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# ANNALS OF INTERNAL MEDICINE

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### DEPARTMENT OF REVIEWS

The Journal will make an especial feature of the review of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.


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# The Pathology of Certain Signs and Symptoms in Primary Carcinoma of the Lung: Illustrative Cases*

By Carl Vernon Weller, M.S., M.D.

In one hundred clinical reports of carcinoma of the lungs (including the bronchi), selected at random from the literature, the various signs and symptoms were mentioned in diminishing order of frequency, as follows: Cough; sputum, usually bloody or blood-streaked at some time, but rarely of the "raspberry jelly" or "currant jelly" type; pain in chest; dyspnoea; loss of weight; osteo-arthropathy, usually in the form of clubbing of the fingers only; pleural effusion, frequently bloody; fever; venous engorgement, or oedema, or both, of the upper portion of the body; disturbances of the central nervous system; hoarseness; anorexia; paralysis of a vocal cord; dysphagia; nausea and vomiting; abdominal pain; inequality of the pupils; inequality of the radial pulses; pain in the arm; sense of pressure in chest; cachexia; cyanosis; pain in lower extremities; stertor; pain in back; headache; chills. In regard to relative frequency, cough is mentioned sixty-one times, the sputum forty-seven times, pain in the chest forty-four times and dyspnoea forty-four times in contrast to the last five items of the list which are each mentioned but once.

It is obvious that a compilation from so many different sources must not be accepted as dogmatically expressing the numerical importance of the various elements in the symptomatology of carcinoma of the lungs and bronchi. Many of the case reports which were used make no pretence of presenting the complete clinical picture. Nevertheless, the list does reveal the manifestations, both subjective and objective, which have been noted in connection with this disease condition and upon which a correct diagnosis was based in some instances, suspected in others, and entirely missed in a group which was altogether too large.

An extensive survey of the literature of primary carcinoma of the lungs and bronchi sustains the belief that the chief cause of inability to diagnose this condition correctly has been failure to keep it constantly in mind in differentiating chest conditions. The belief still held by many that primary carcinoma of the lung is an exceedingly rare condition, not to be encountered in a lifetime of

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ordinary medical practice, is to blame for this unconscious exclusion. When it is realized that at the present time, in Europe and in America, primary carcinoma of the lungs and bronchi is found once in every 200 autopsies upon adults and once in every twenty deaths from carcinoma (1), its importance will be appreciated and the possibility of its being present will always be entertained, especially if the patient be a male (74 per cent of all cases) in the fifth, sixth or seventh decades of life.

Inspection of the list of signs and symptoms gathered from the 100 random case reports of carcinoma of the lung shows that those near the head of the list are such as are of evident relationship to the primary lesion in the respiratory tract. Those near the foot of the list have a less obvious connection, some of them being secondary or indirect effects. If those cases are studied in which the diagnosis is not made until autopsy, it will be found that many of them have shown as important presenting signs and symptoms one or more of those which are relatively rarely mentioned in clinical case reports. It is especially important, therefore, to call attention to the occurrence of these more remote effects. This will be done by presenting the histories of twelve cases of primary carcinoma of the lungs and bronchi in which diagnosis was confirmed or established by autopsy in the Department of Pathology of the University of Michigan. Only one (2) of these cases (No. 1) has been published previously. The pathological basis for the signs and symptoms which suggested carcinoma of the lungs, or should have done so in the undiagnosed cases, will be described in so far as it was ascertainable.

Physical findings are not included in the above list. They are oftentimes of great importance but usually change so decidedly in the course of the disease that they do not lend themselves well to analysis. The increasing area of dulness corresponding to the neoplasm itself, is a practically constant finding in the more advanced cases but the lung parenchyma peripheral to a carcinoma at the hilus may give a great variety of signs depending upon whether atelectasis, bronchiectasis, chronic fibroid pneumonia, neoplastic infiltration or surrounding pleural effusion is the determining factor.

It must be understood that the use or neglect of the two greatest aids in the diagnosis of primary malignancy of the lung is not primarily under discussion here. These are *bronchoscopy* (3) for direct inspection and probatory excision; and *roentgenoscopy* (4), particularly with the use of special means to aid visualization (pneumothorax, lipiodol, iodipin). Upon these two procedures much dependence must be placed in making a positive diagnosis. Neither of these, however, is to be entered upon lightly. It is now well recognized that lipiodol may remain for weeks or months in the bronchioles and alveoli and give rise to a foreign body reaction. Aortic aneurism, in particular, is an important contra-indication to bronchoscopy and should be ruled out by every possible means (3). Signs and symptoms must be present in a kind and to a degree which raises a strong pre-

sumption of malignancy or other grave pathology before these measures are utilized.

Review of the list of signs and symptoms given above will show that there is not one of them which, taken alone, is pathognostic of primary malignant disease of the lung. They may be considered as indicating roughly four groups of pathological processes:

1. Signs and symptoms due chiefly to local primary pathology.
   - Cough
   - Pain in chest
   - Sputum
   - Dyspnoea
   - Cyanosis
   - Dysphagia
   - Stertor
   - Effusion
2. Signs and symptoms of mediastinal tumor:
   - Cough
   - Pain in chest
   - Dyspnoea
   - Cyanosis
   - Venous engorgement and oedema of the upper part of the body.
   - Recurrent laryngeal paralysis
   - Hoarseness
   - Inequality of pupils
   - Inequality of radial pulses
   - Abdominal pain
   - Dysphagia
   - Stertor
3. General systemic effects:
   - Loss of weight
   - Weakness
   - Osteo-arthropathy (clubbing of fingers)
   - Fever
   - Chills
   - Cachexia
   - Anorexia
   - Nausea and vomiting
4. Signs and symptoms frequently associated with metastasis:
   - Evidence of central nervous system lesions
   - Pain in lower extremities
   - Pain in back
   - Abdominal pain
   - Headache

Of the twelve cases reported here four only were correctly diagnosed during life, although one other was considered to be intrathoracic malignancy, probably lymphosarcoma, and two were diagnosed as abdominal malignancy. It must be recalled that this series of cases begins in 1911. There has been a noticeable improvement in ability to diagnose primary carcinoma of the lungs and bronchi since that time. This is apparent in the abundant literature which has accumulated as well as in our local experience. In part, this gratifying improvement has been due to the more general clinical awareness of the relative frequency of the condition in question, and in part to the perfection and application of the special methods of investigation and confirmation to which reference has already been made. One can conclude that the successful *intra vitam* diagnosis of this condition involves a sequence of three steps: (a) The more or less constant inclusion of this condition in the list to be differentiated when obscure pathological conditions in the adult are being differentiated; (b) the recognition of certain signs and symptoms which raise such a strong pre-

sumption in favor of the diagnosis; that (c) special investigations are carried out which strongly support or confirm the diagnosis. The pathological processes producing the signs and symptoms entering into the second step form the basis of this study. In reviewing the following cases an attempt will be made, through the correlation of the pathological changes found at autopsy with the presenting signs and symptoms, to ascertain what opportunity, if any, of arriving at a correct diagnosis was offered. This is done without any intention of implying that a correct diagnosis *should* have been made in any particular case. Diagnosis by retrospection is notoriously easy and the advantage gained by the backward look has become proverbial.

CASE 1

COMA, CYANOSIS, DYSPNEA

*Clinical Abstract* (5). An awning-maker, 47 years old, was brought to the hospital in coma. Only a meager history could be obtained from the patient's friends. For two years he had not been as well as formerly and had had marked dyspnea for some time, with epistaxis and hemoptysis. The patient had believed that he had asthma, and stramonium leaves were found in his pockets. He had slipped to the floor, unconscious, while seated in a chair in a hotel lobby.

Examination in the Department of Internal Medicine showed the patient to be intensely cyanotic, the skin dry, and the pupils evenly and markedly contracted, reacting but very little to light. There was marked dyspnoea with great activity of the accessory muscles, and respiration was characterized by a short deep inspiration and long expiratory period. The rate was but 10 to 12 per minute. There were many inspiratory râles. No area of dulness was detected. The patient moved both arms but no spontaneous movements of the legs were noted. The rectal temperature was 97.8° and 96° F.

Upon these findings a tentative diagnosis of morphin poisoning was made and treatment instituted accordingly. (Subsequent examination of the stomach washings showed no morphin.) Oxygen was used in an attempt to relieve the cyanosis and dyspnoea, but without effect. The patient died four hours after entering the hospital.

*Autopsy.* (A-352.) No free gas or fluid was found in the pleural cavities. There were a few pleural adhesions, most marked at the right apex. The anterior border of the left lung reached the left parasternal line. The large bronchi of this lung were filled with creamy pus. The bronchial nodes on the left were small, heavily pigmented and showed no neoplasm. The anterior border of the right lung reached the right parasternal line. This lung was firmly bound to a tumor mass the size of an orange which included the right bronchial nodes, the esophagus and the descending aorta. This tumor mass completely surrounded the main bronchus to the right lung and the bronchial wall was infiltrated and destroyed. At this point the lumen of the bronchus was markedly narrowed. At the level of the bifurcation, the trachea showed a nearly complete stenosis, admitting only a 2 mm. rod. This stenosis was due to the neoplasm mass compressing and infiltrating the trachea from without. Aside from the regional lymph nodes the only metastases found were in the left kidney. Microscopical examination showed the neoplasm to be a mucin-producing cylindric-celled adenocarcinoma.

*Pathological Diagnosis.* Stenosing primary adenocarcinoma of right main bronchus. Metastases in bronchial lymph nodes and left kidney. Acute stenosis of trachea. Partial stricture of esophagus. Chronic purulent fibroid pneumonia. Bronchiectasis. Emphysema. Chronic leptomeningitis. Atrophy with acute and chronic passive congestion of all organs.

*Comment.* In this instance there was no opportunity for detailed clin-

ical study. The presence of pinpoint pupils led to a strong suspicion of morphinism and emergency treatment for that possibility was indicated. Autopsy showed that death was due to asphyxiation from stenosis of the right main bronchus by neoplastic infiltration, and of the trachea, by neoplastic compression. The coma, cyanosis and dyspnea, which were the other important signs and symptoms, thus found their explanation. It is probable that the contraction of the pupils was due to lesion of the sympathetic chain by the infiltrating new growth, although it is extremely rare for the pupillary change to be bilaterally symmetrical. Survey of the case in retrospect shows a history of ill health for two years, dyspnea and hemoptysis, then extreme cyanosis, pupillary changes and coma from acute asphyxiation as the signs and symptoms. The clinical manifestations are thus seen to be in accord with those listed above. The nearly complete obliteration of the trachea explained the lack of clinical improvement when oxygen was administered.

CASE 2

ABDOMINAL PAIN

*Clinical Abstract.* A man, 57 years of age, giving his occupation as "bridgeman," first entered the Department of Dermatology and Syphilology complaining of sharp, intermittent pain in the upper left abdominal quadrant. The pain was worse when lying down and had no relation to the taking of food. There had been no nausea or vomiting. The patient was believed to have acquired both gonorrhea and syphilis twelve years before, but a course of arsphenamin treatment failed to influence the pain favorably and the patient continued to lose weight. Physical examination did not show evidence of disease of the thoracic organs. Because of the location of the pain, constipation, a history of blood in the stools and X-ray evidence of some obstruction of the colon in the region of the splenic flexture when examined after a barium enema, the patient was transferred to Surgery where a diagnosis of carcinoma of the splenic flexure was accepted. Laparotomy was done and the colon was found to be moderately constricted by firm fibrous adhesions. These were cut. There was no neoplasm.

The patient was discharged from the Hospital about three weeks after this operation, still complaining of pain in the upper left quadrant and 'weakness' of the back. At home the pain grew worse and he continued to lose weight, so he returned to the Hospital after 15 days. A gently rounded swelling was now found over the left half of the back, extending from the fifth to the eighth rib. This gave the first indication of intra-thoracic pathology. Examination in the Department of Roentgenology showed the left half of the thorax to be everywhere more dense than the corresponding areas upon the right. The greatest density occurred at the level of the ninth and tenth ribs posteriorly and in this region the shadow of these ribs could not be made out. There was increased density of the hilus also. Neoplasm of the thoracic wall was diagnosed. The tumor mass on the back increased in size rapidly and the patient died 12 days after his second admission and 14 months after the onset of his illness.

*Autopsy.* (A-1140.) Externally the body showed a large subcutaneous mass, located over, and apparently involving the left posterior portions of the fifth to eighth ribs. This area showed no ulceration and the skin moved freely over the mass. The laparotomy wound was represented by a well-healed scar. The left lung was found to be heavily infiltrated at the hilus by a new growth which extended posteriorly and laterally to the thoracic wall where the lung was firmly adherent. The fifth to eighth ribs in this region were extensively infiltrated by the neoplasm and showed several fractures. Multiple metastases were

found as listed in the diagnosis which follows.

*Pathological Diagnosis.* Primary adenocarcinoma of bronchus of third order to lower lobe of left lung, with direct extension through thoracic wall. Multiple metastases in lungs, bronchial and prevertebral lymph nodes, pleura, diaphragm, periosteum of ribs, heart muscle, liver, kidneys, spleen and retroperitoneal nodes. Bronchiectasis. Emphysema. Purulent lobular pneumonia. Hemorrhagic infarct of lungs. Fatty heart. Atherosclerosis of aorta. Brown atrophy of liver. Passive congestion and parenchymatous degeneration of all organs. Completely healed laparotomy scar.

*Comment.* This case is typical for that group of primary carcinomas of the lungs and bronchi in which attention is focused upon the abdomen because of referred pain. In this instance the pain seems to have been due to the direct extension of the neoplasm into, and finally through, the thoracic wall. Only with the appearance of the sub-cutaneous neoplasm in the left back was X-ray examination of the lung fields done. Earlier utilization of this aid would have forestalled the laparotomy which was unnecessary, for the pain in the upper left quadrant was entirely independent of the adhesions which were freed at that operation.

### Case 3

### Vomiting, Abdominal Pain, Loss of Weight

*Clinical Abstract.* Clinical information is incomplete in regard to this case. The patient was a coal miner, 67 years of age, who entered the Department of Internal Medicine complaining of vomiting, abdominal pain and loss of weight. There was marked enlargement of the liver and some dysphagia. A diagnosis of abdominal malignancy, either of the cardiac end of the stomach or lower oesophagus, was made. The condition was thought to be inoperable and the patient died soon after entering the Hospital.

*Autopsy.* (A-1162.) External examination of the body showed an enlarged lymph node at the base of the neck on the left side. The right pleural cavity contained a large amount of bloody fluid. The pericardial sac was infiltrated on the mediastinal side by a neoplasm which extended into the wall of the auricle. The left lung grossly showed no neoplasm except a pleural plaque near the hilus. The root of the right lung was occupied by a large mass which extended particularly along the main bronchus to the lower lobe. This bronchus was infiltrated and compressed by the surrounding neoplasm so that its lumen was completely obliterated for some distance. The pleura on the right side showed many nodules of new growth. About 4.5 cms. below the level of the tracheal bifurcation the wall of the esophagus was infiltrated from without and at this point the lumen was distorted and there was a small traction diverticulum. The liver showed numerous metastases up to 3 cms. in diameter.

*Pathological Diagnosis.* Primary medullary carcinoma of main bronchus to lower lobe of right lung. Metastatic carcinomatosis of both lungs, bronchial nodes and mediastinum with extension to pericardium and to wall of esophagus. Traction diverticulum of esophagus. Metastases in liver, retroperitoneal and left cervical nodes. Anthracosis. Bronchiectasis. Chronic purulent bronchitis. Pulmonary infarction with beginning gangrene. Bronchopneumonia. Emphysema. Edema and passive congestion of the lungs. Brown atrophy of heart. Old syphilitic myocarditis of left ventricle. Sclerosis of coronaries and aortic cusps. Chronic passive congestion, atrophy and parenchymatous degeneration of all organs. Aortic atherosclerosis upon a syphilitic basis. Left-sided pyelonephrosis with nephrolithiasis. Dilatation of left ureter. Chronic pyelitis, ureteritis, cystitis and prostatitis. Orchitis fibrosa syphilitica. Lipoidosis of adrenals. Multiple anomalies of ribs.

*Comment.* As in the preceding case the clinical manifestations led to a diagnosis of abdominal malignancy. Compression, distortion and traction diverticulum of the lower esophagus, together with liver metastases provided the anatomical basis inducing this incorrect interpretation. A "sentinel" node above the inner third of the left clavicle seemed to confirm this opinion. It must be remembered that carcinoma of the lung also frequently shows early metastasis by way of the ascending lymphatic trunks. This case closely resembles the third one in the series reported by Barron (6). A male patient, 52 years old, had as his only clinical findings pain in the stomach, anorexia, vomiting after each meal and loss of weight and strength. At autopsy an adenocarcinoma was found at the hilus of the right lung and there were metastases in the brain. Such patients frequently are asked to submit to laparotomy and the diagnosis may never be cleared up without autopsy.

### Case 4

### Pain in Legs

*Clinical Abstract.* A farmer, 40 years old, entered the Neurology Service of the University Hospital because of pains in the legs. This symptom began ten months before entrance and gradually became unbearable. He had been taking as much as three grains of morphin sulphate at a dose in order to get partial relief. There had been some pain in the lower back also, but this was of minor importance to the patient. During the past three weeks first the left leg and then the right had become edematous. There had been neither dyspnoea nor hemoptysis at any time. X-ray examination gave positive evidence of malignancy of the left lung and a diagnosis of carcinoma of the lung with metastases to the spine was made. At the insistence of the patient that something be done to relieve the pain in his legs he was transferred to Surgery for anterolateral chordotomy. Following the operation, which accomplished this purpose, pain in the upper abdomen and chest became more severe, external dorsal decubitus developed and the patient died five weeks after the operation, and approximately one year after the onset of the pain.

*Autopsy.* (A-1500.) Externally the body showed the well-healed scar of a surgical incision extending 13 cms. downward from the base of the neck, the site of the chordotomy operation. All of the bony prominences on the dorsal surface of the body were marked by areas of decubitus, the largest of these, over the sacrum, measuring 12 by 18 cms. The left lung was firmly adherent over its upper one-third. In the adhesions and in the free pleura of the lower portion of the lung there were numerous nodules of neoplasm. The bronchus to the upper lobe was occluded by a mass of neoplasm which infiltrated its wall and extended peripherally in the peribronchial tissue. The remainder of the lung contained many smaller neoplastic masses which were confluent in the upper lobe but discrete toward the base. Neoplasm was not found, either macroscopically or microscopically, in the vertebrae. The pre-vertebral retroperitoneal lymph nodes contained many metastases, even as low as in the lumbar region. Some of these large nodes lay in contact with and pressing upon, branches of the lumbosacral plexus. There was no neoplastic infiltration of the spinal meninges or of the cord itself at the levels which were examined microscopically.

*Pathological Diagnosis.* Primary medullary mucoid adenocarcinoma of bronchus to upper lobe of left lung. Stenosis of bronchus. Infiltration and lymphogenous metastasis throughout the left lung. Metastases in bronchial, mediastinal, lower cervical, prevertebral and retroperitoneal lymph nodes, right lung and liver. Septicopyemia. Multiple abscesses in lungs with gangrene and purulent pneumonia. Multiple abscesses in kidneys with metastatic descending purulent

pyelonephritis, ureteritis, cystitis and urethritis. Terminal infection secondary to thoracic chordotomy. Thrombosis of pulmonary vessels, vena cava, external and internal iliac veins and vesical plexus. Anemic infarcts in kidneys. Congestion and edema of lower extremities. Relative tricuspid and pulmonary insufficiency. Passive congestion, atrophy and parenchymatous degeneration of all organs. Serous atrophy of all adipose tissue. Colloid goiter. Old orchitis.

*Comment.* Pain in the legs dominated the entire clinical picture of this case. X-ray examination of the chest reevaled the primary source of the neoplasm which had never produced immediate signs or symptoms. That the pain in the legs was due to vertebral metastases was a clinical inference unsupported by evidence of a destructive lesion. There had been no evidence of a compression myelitis and microscopical examination of the vertebrae showed them to be free from neoplasm. Lymphogenous metastases among the nerves forming the lumbosacral plexus furnished the anatomical basis for an explanation of the pain. Edema of the legs was associated with thrombosis of the iliac veins. At the time of death this process had ascended for some distance in the inferior vena cava. Venous obstruction from the enlarged nodes filled with neoplasm made this thrombosis possible.

### Case 5

#### Engorgement of Superficial Veins, Hoarseness

*Clinical Abstract.* A farmer, age 56, was admitted to the Department of Internal Medicine of the University Hospital with his chief complaints swelling of the neck, difficulty in swallowing and pain in the back. He stated that his trouble began three months before with hoarseness which was soon followed by swelling of the right side of the neck. He experienced greater difficulty in swallowing liquids than solids. Later dyspnea and a dry cough developed. He had not had hemoptysis. For two weeks there had been some impairment of vision in the right eye. Examination showed a scar on the upper left thorax anteriorly, extending over the shoulder, the site of an accidental wound with an ax. There was a marked distension of the veins of the neck and the superficial veins of the front of the chest and upper half of the abdomen. (See Figure 1.) The superficial venules were dilated along the line of the insertion of the diaphragm. There was marked dulness over the right chest from the second interspace up. The cervical glands were enlarged and hard on the right, a nodular mass filling the supraclavicular fossa; much less so on the left. The right arm was edematous. The Department of Otology reported a bilateral recurrent laryngeal paralysis. X-ray examination showed a very high diaphragm on the right, widening of the mediastinal shadow and haziness of the right apex. (See Figure 2.) A diagnosis of mediastinal tumor, probably lymphosarcoma, with mechanical obstruction of the superior vena cava, was made. The masses in the neck and the mediastinum were treated with X-rays without any relief. The difficulty in swallowing increased and the superficial venous engorgement became more marked. Death occurred eighteen days after admission.

*Autopsy.* (A-1760.) The brain showed a tumor mass in the right choroid plexus. The right pleural cavity contained 1500 cc. of yellowish fluid without evidence of blood. On the left, 900 cc. of similar fluid was found. The upper portion of the mediastinum was filled with a firm nodular neoplasm which extended especially toward the right along and above the clavicle and the first rib. At the base of the heart in the pericardial reflexions about the great vessels several small nodules were found. To the naked eye, there was no neoplasm in the left lung. The right lung, how-

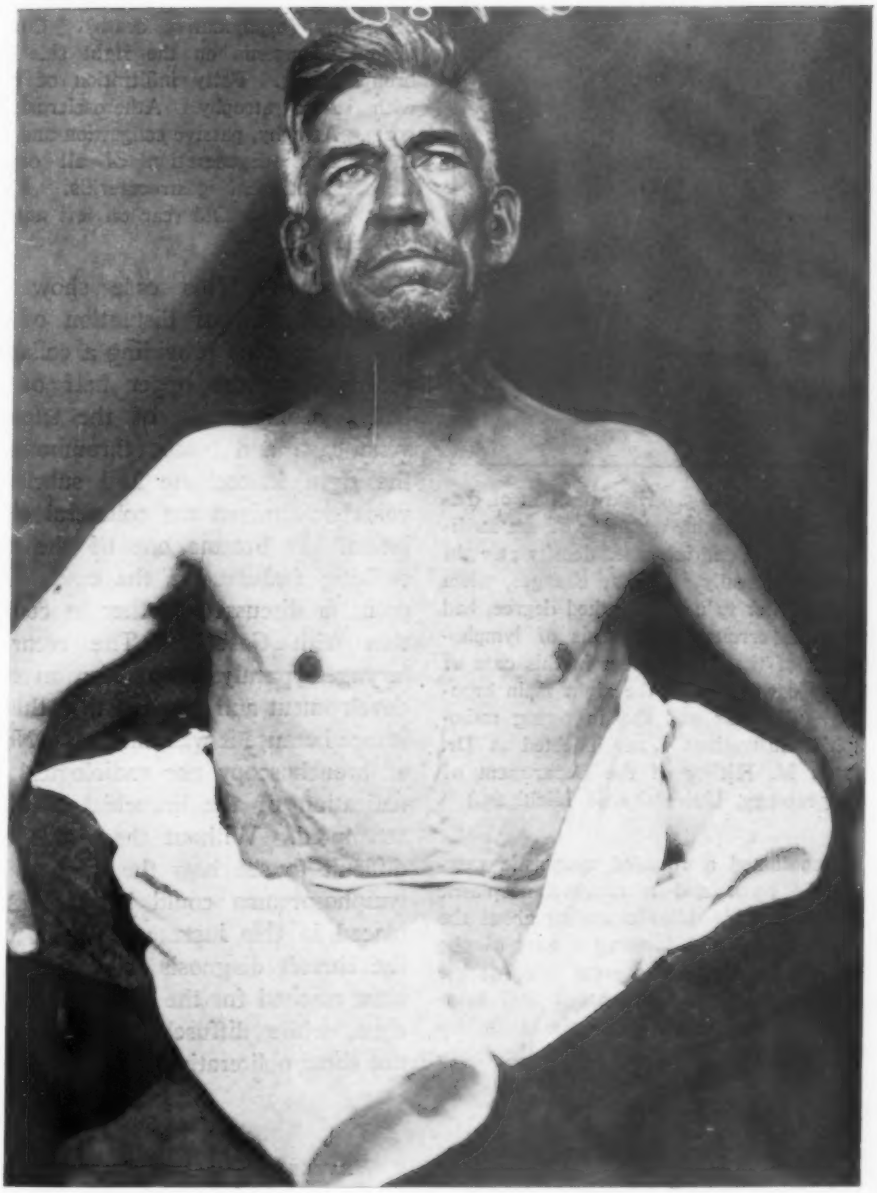

FIGURE 1. Case 5. Engorgement of the veins of the neck and of the superficial veins of the thorax and upper abdomen. Collateral venous circulation produced by compression of the superior vena cava and thrombosis of the right innominate and subclavian veins.

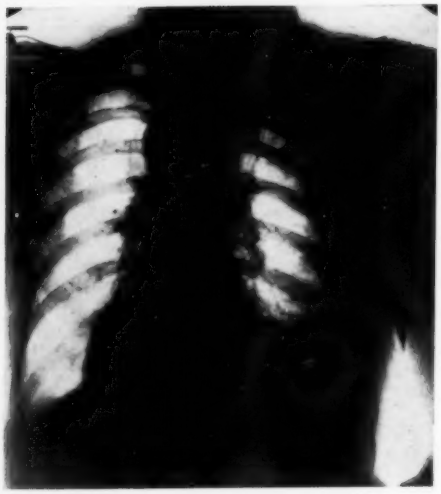

FIGURE 2. Case 5. High position of diaphragm on the right, widening of the mediastinal shadow and increased density at right apex and laterally. Similar changes, when present earlier to a less marked degree, had led to the erroneous diagnosis of lymphosarcoma of the mediastinum in this case of primary carcinoma of the right main bronchus. (For this and the following radiographic illustrations I am indebted to Dr. Preston M. Hickey of the Department of Roentgenology, University of Michigan.)

ever, contained a rounded neoplastic mass near the apex and a massive neoplastic induration at the hilus centering about the main bronchus and forming a part of the mediastinal tumor. The great veins of the upper thorax were surrounded and compressed by neoplasm, while the right innominate vein showed a tumor thrombus. Metastases were found as listed in the summary which follows.

*Pathological Diagnosis.* Primary scirrhous carcinoma of the right main bronchus with direct extension into the mediastinum and along the great vessels into the right shoulder. General carcinomatosis of bronchial nodes, lungs, thyroid and prevertebral, retroperitoneal and mesenteric lymph nodes. Hematogenous metastases into choroid plexus, spleen, liver, kidneys, adrenals, pancreas and prostate. Thrombosis of right innominate and subclavian veins. Edema of glottis (asphyxiative death). Chronic fibroid pneumonia on the right side with bronchiectasis. Fatty infiltration of heart with serous atrophy. Atherosclerosis of aorta. Atrophy, passive congestion and parenchymatous degeneration of all organs. Chronic catarrhal gastroenteritis. Right-sided hydrocele. Old scar on left anterior thoracic wall.

*Comment.* This case showed a marked degree of distention of the superficial veins providing a collateral return from the upper half of the body. Compression of the superior vena cava and tumor thrombosis of the right innominate and subclavian veins determined the collateral circulation. It became one of the most striking features of the case. This point is discussed further in connection with Case 7. The recurrent laryngeal paralysis was also an early development and is unusual in this instance because it was bilateral. Neither bronchoscopy nor radiological visualization of the bronchial tree was attempted. Without these aids it is difficult to see how the diagnosis of lymphosarcoma could have been replaced in this instance. With them, the correct diagnosis might not have been reached for the right main bronchus, while diffusely infiltrated, did not show obliteration or even stenosis.

### CASE 6

### WEAKNESS, ENLARGED CERVICAL NODE

*Clinical Abstract.* A janitor, age 65, entered the Department of Internal Medicine complaining of a "tired feeling," weakness, a slight cough, occasional precordial pain and swelling of the extremities. He considered the onset of his illness to have occurred six months earlier when he found

that he felt tired all of the time, even after sleeping. The slight cough had recently produced a small amount of blood-streaked sputum. He had lost twenty-five pounds in weight during his illness. Examination showed a slightly tender, smooth, firm, freely movable mass, measuring 3 by 2 by 2 cms., in the right supraclavicular fossa. The patient said that this had appeared about a week before. It was removed for microscopical examination and proved to be a lymph node replaced by metastatic cystadenocarcinoma. There was a slight clubbing of the fingers. Upon X-ray examination the entire right lung field was found to show increased density with a rounded mass of greater opacity nearly filling the apex. Below this there were other areas of increased density. In the left lung field there was increased density only about the hilus. On subsequent examinations these areas of density were found to be increasing in size. A diagnosis of adenocarcinoma of the right lung with metastases was made. A series of deep X-ray treatments was given without producing favorable change in the progress of the neoplasm. Slight rise in temperature each day, gradual loss of weight and strength, periods of irrationality and general convulsions characterized the remainder of his stay in the Hospital. He died six months after admission and about one year after the supposed onset of his illness.

*Autopsy.* (A-1760.) Examination of the brain showed marked atrophy, congestion and edema, without evidence of neoplasm. The left lung was grossly negative in respect to neoplasm, but the right lung, which showed a complete adhesive pleuritis, was filled in the upper and middle lobes with masses of new growth showing central necrosis. These were fewer and smaller in the lower lobe. The wall of the main bronchus on the right was greatly thickened and was in continuity with large tumor masses spreading radially into the substance of the lung.

*Pathological Diagnosis.* Primary adenocarcinoma mucosum of right main bronchus with metastases in bronchial, cervical and mediastinal lymph nodes and left fifth rib. Encapsulated fibrino-purulent empyema on the right side. Chronic adhesive pleuritis. Marked tumor cachexia. Atrophy, passive congestion and parenchymatous degeneration of all organs. Marked serous atrophy of all fat tissue. Marked atherosclerosis of the aorta. Secondary contracted kidney. Chronic prostatitis with cystic glandular hyperplasia. Chronic purulent posterior urethritis and cystitis. Chronic hypertrophic spondylitis with lordosis of lumbar vertebrae. Chronic focal leptomeningitis with cerebral atrophy.

*Comment.* An enlarged cervical node, removed for microscopical examination proved the malignant nature of the essential pathology in this case. Clear-cut roentgenological findings, checked by negative studies of the gastrointestinal tract, served to localize correctly the process. The cerebral changes in the latter course of the disease were not due to metastases as might well have been the case, but rather to the low grade renal insufficiency and to tumor cachexia.

### Case 7

#### Pain in Arms and Chest, Hoarseness, Pupillary Inequality

*Clinical Abstract.* A laborer, 49 years of age, complained especially of pain in the arms, commencing one and one-half years before admission to the Department of Internal Medicine. At first this pain was in the right arm and shoulder; later it spread to the other arm, the chest and the back, but never went below the waist line. With the pain there had been shortness of breath. A few months earlier, for a period of about two weeks, his neck, shoulders and arms had been much swollen and pitted on pressure. There had been a loss in weight of 25 pounds during two months. The patient stated that he had suddenly "lost his voice" in the preceding summer and it had been husky ever since

that time. He had noticed also that his left eyelid drooped. There had been no hemoptysis.

Examination showed the thorax to be deep and wide with expansion greater upon the left than upon the right. Over the upper sternum there was a large, rounded, hard mass, non-pulsating, slightly to the left of the midline. The veins of the anterior thoracic and abdominal wall were distended and there was a visible pulsation extending from the jugular to the superficial epigastric vessels. This was more marked upon coughing. There was no tracheal tug. The lungs showed dulness at the right apex and also at both the left apex and the left base. In addition to the drooping of the left lid with consequent narrowing of the palpebral fissure, it was found that the left pupil was smaller than the right and did not dilate well on cervical stimulation. It was believed in the Department of Neurology that these findings were indicative of a compression lesion of the left cervical sympathetic. There was also a complete paralysis of the left vocal cord. The X-ray findings were those of a non-pulsating mediastinal tumor mass, eroding the sternum, with bilateral pleural effusion. (See Figure 3.) The final diagnosis was mediastinal neoplasm, probably carcinoma of the lung.

The pleural effusion, which was blood tinged, was removed from the chest but it returned repeatedly. The mediastinal area was given roentgen irradiation both anteriorly and posteriorly. There seemed to be temporary relief from the pain but the progressive growth of the neoplasm was unchecked. The pain in the chest and arms returned with even greater severity and the patient died three months after entering the Hospital and a year and nine months after the onset of his illness.

*Autopsy.* (A-2140.) At autopsy a smoothly rounded, ovoid mass, 7 cms. in its longitudinal diameter and 10 cms. transversely, elevated 3 cms. above the surrounding surface, was found to occupy the region of the upper portion of the sternum. The overlying skin was not ulcerated and the mass was firm and but slightly yielding to pressure. Upon removing the integument, this mass was found to extend from the supra-sternal notch to the level of the third intercostal space and laterally 6.5 cms. to the right of the midline and 6 cms. to the left. The left pleural cavity contained 2500 cc. of blood stained fluid and the right, 1500 cc. The sternum, with the neoplasm infiltrating it, was removed en masse with the thoracic viscera. Beneath the sternum the neoplasm formed a mass about 8 cms. in diameter. On the left it invaded the pericardium about the great vessels. Laterally it was firmly bound to the upper lobe of the right lung and it also extended in the left lung to its apex. The superior vena cava was penetrated and within its lumen the neoplasm extended as a completely occluding mass to, but not into, the cavity of the auricle. The neoplasm thrombus extended above into both internal jugular veins. The trachea and large bronchi were patent throughout and showed no infiltration by the new

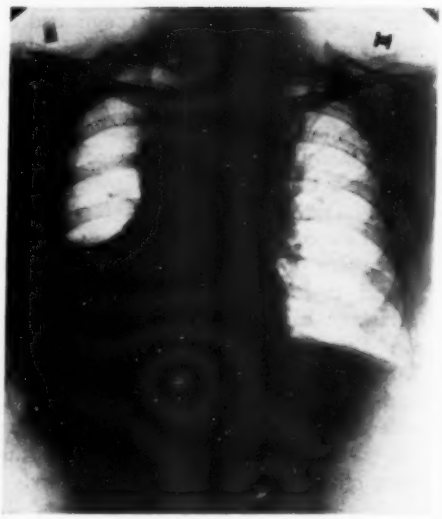

FIGURE 3. Case 7. Widening of mediastinum and bilateral pleural effusion, more abundant on the left; diagnosed mediastinal neoplasm. At autopsy primary medullary adenocarcinoma of upper lobe of right lung, arising in an area adjacent to the mediastinum, was found.

growth. The pericardial sac was heavily infiltrated and there were metastases to both visceral and parietal surfaces. Pleural metastases were found over both lungs and extensions into both lungs, but the chief pulmonary mass was in the upper right lobe which was firmly united to the under surface of the sternum.

Microscopical examination showed the neoplasm to be a carcinoma varying from medullary adenocarcinoma to scirrhous adenocarcinoma in type. It had arisen well out in the substance of the lung, apparently in an area of chronic fibroid pneumonia.

*Pathological Diagnosis.* Primary medullary adenocarcinoma of upper lobe of right lung, arising in an area of old fibroid pneumonia. Direct extension through pleura, tissues of chest wall, sternum and about superior vena cava and aortic arch. Tumor thrombosis of superior vena cava. Thrombosis of both internal jugular veins. Retrograde lymphogenous metastasis downward through prevertebral chain as far as the semilunar ganglia. Bilateral hemohydrothorax. Atrophy, passive congestion and parenchymatous degeneration of all organs.

*Comment.* Throughout its course this example of primary carcinoma of the lung was characterized by pain in the shoulders, arms and chest. The early perforation of the sternum was an unusual feature, for carcinoma of the lungs usually kills before there is direct extension through the thoracic wall. However, Bruecken (7) described a patient upon whom a diagnosis first of gumma of the sternum, and later of sarcoma of the sternum, had been made because of a similar picture. Kikuth (8) found a mass the size of an apple in the left pectoralis muscles in direct continuity with a primary carcinoma of the lung. The large mediastinal mass in Case 7 produced the complete group of left-sided nerve signs; drooping of the eyelid, contraction of the pupil and recurrent laryngeal paralysis. As in Case 5 the utilization of the superficial veins as a collateral venous return from the upper half of the body was an important sign. A temporary engorgement of the neck, shoulders and arms marked the period when this collateral circulation was becoming established. Tumor thrombosis had obturated completely the superior vena cava. This important sign in connection with carcinoma of the lungs and bronchi has been studied especially by Dana and McIntosh (9) who were able to show that in almost all examples of thrombosis of the superior vena cava in association with primary carcinoma of the lung the carcinoma will be found to arise in the right lung, as was true in our present case.

### Case 8

#### Pain in the Back, Paralysis of Lower Extremities, "Pott's Disease"

*Clinical Abstract.* A female school teacher, age 40, was brought to the Orthopedic Surgery service on a Bradford frame, for pain in the back and paralysis of the lower extremities. The patient had first noticed pain in her back 14 months before. The pain was sharp in character and radiated toward the anterior abdominal wall. She had consulted a physician for this pain for the first time seven months before. X-ray examination at that time demonstrated a destructive lesion of the tenth thoracic vertebra which she was told was tuberculous. A plaster jacket was applied and the patient continued teaching until the severity of the symptoms compelled her to stop. She soon began to sense numbness in the feet and legs and then entered a tuberculosis sanatorium where she remained for five months. Shortly after admission to this sanatorium she attempted to get

out of bed and fell. This caused severe pain in the back and within two days she had practically complete paralysis of the lower extremities with loss of control of rectal and vesical sphincters. The paralysis increased rapidly and within a week there was a complete loss of power of motion and of sensation from the umbilicus down. X-ray examination now showed destruction of the ninth, tenth and eleventh thoracic vertebrae with rarefaction of the lower vertebral bodies. There was destruction of the right tenth rib at its articulation to the spine with a loss of about two inches of its substance. A well outlined and dense shadow extended laterally on both sides of the spine from the ninth to the twelfth thoracic vertebrae. Throughout the entire lumbar spine, the sacrum and the ilium there were areas of decreased density and of increased density, such as are found in a combined osteoclastic and osteoblastic malignancy. Externally, a fluctuating swelling developed to the left of the tenth thoracic vertebra. This was incised and bloody, non-coagulating fluid escaped. A diagnosis of malignant disease of the spine was made.

In this condition the patient entered the University Hospital. The fluctuating swelling in the back having reappeared, it was incised and neoplastic tissue infiltrating the vertebral laminae found. A small portion was taken for microscopical examination. This showed a very vascular tissue infiltrated with small round cells. A tentative diagnosis of hemangiosarcoma of the spine was returned, and X-ray therapy was instituted. A week later the patient developed signs of lobular pneumonia and died two weeks after entering the University Hospital and approximately fifteen months after the supposed onset of her symptoms.

*Autopsy.* (A-2284.) Aside from the recent surgical incision the external examination of the body showed nothing of significance. At the mesial border of the lower lobe of the left lung a neoplastic nodule 3 cms. in diameter was found. This was adherent to the vertebral column at the level of the ninth thoracic. The prevertebral fascia and the bodies of the vertebrae were infiltrated with neoplasm. At the end of the autopsy the neoplasm was still considered to be of the sarcoma group, primary in the vertebrae and infiltrating the lung by extension. Microscopical examination showed that the contrary was the case. The oldest area was found to be in the mass in the lung and the greater part of the growth was a papilliferous adenocarcinoma which became scirrhous in areas. The tentative interpretation of the portion removed at operation was erroneous.

*Pathological Diagnosis.* Primary bronchial papilliferous adenocarcinoma scirrhosum of the lower left lobe with direct extension through the pleura into the vertebral fascia and vertebrae and with multiple hematogenous metastases in bones (vertebrae and pelvis) and liver. Generalized lymphogenous metastases in bronchial nodes and lungs. Transverse myelitis. Acute lobular pneumonia. Atrophy, chronic passive congestion and parenchymatous degeneration of all organs. Old healed glomerular-tubular nephritis. Marked lipoidosis of adrenals. Thrombosis of pampiniform plexus. Multiple pulmonary emboli. Hyaline leiomyofibroma.

*Comment.* The lung shares with other organs, but particularly the prostate and the thyroid, the possibility of being the primary site of a hidden carcinoma which produces bone metastases to dominate the clinical picture. In this case the vertebral involvement was in part by direct extension and in part by metastasis. With a fairly sharply localized involvement of the vertebral column the diagnosis is apt to be Pott's disease as it was in this instance. This case is much like the thirteenth case in the series reported by Barron (10). A man, 46 years old, experienced a sudden pain in the back while playing golf and a deformity developed at once. Pain in the legs and weakness

became worse under chiropractic treatment. Pott's disease was diagnosed and he was admitted to a tuberculosis sanitorium. He had then a knuckle deformity at the twelfth thoracic. At autopsy a scirrhous carcinoma of the left lung was found.

This case was the only instance of primary carcinoma of the lung in a female in our series of twelve. Summation of statistics as given in the literature indicates a sex incidence ratio of 2.8 male to 1 female.

### Case 9

#### Pain in Feet and Legs, Confusion With Aortic Aneurism

*Clinical Abstract.* A negro laborer, age 38, entered the Bone and Joint Out-patient Department of the University Hospital on November 3rd, 1926, complaining of pain in the feet and legs. This had been present since early in September and had become progressively worse. At first it was located in the feet and ankles, but later involved the knees and was described as of sharp shooting character rather than aching. Influenced, perhaps, by a history of gonorrhea, a diagnosis of infectious arthritis with spurs was made. The patient had acquired syphilis at the same time as his gonorrheal infection. Examination at the time of entrance showed no cardiac enlargement but a loud systolic murmur and the aortic second sound was altered in character. There was a slight increase in retromanubrial dulness. There had been occasional cough and night sweats. The Wassermann was two plus. On subsequent examinations a rapid evolution of the disease process was noted. On November 22nd a slight increase in the retromanubrial dulness to the right was noted and there was a marked heaving of the precordium. There was slight dulness at the right apex both anteriorly and posteriorly. A slight tracheal tug was suspected. The liver was large and hard. A week later there was a brassy cough and slight clubbing of the fingers. At this time the patient was discharged against advice with a diagnosis of tertiary lues, syphilis of the liver, syphilis of the aorta with aneurism, and infectious arthritis.

On December 26th the patient returned as an emergency case with all symptoms greatly increased. The liver had become enormous in size. There was now well-marked dyspnea and the cough had increased. The veins of the neck were distended. The area of retromanubrial dulness had increased greatly in size. There was limited expansion of the right chest with dulness posteriorly toward the base, decreased tactile fremitus and increased voice and breath sounds.

Roentgenological examinations showed the progress of the disease. On November 23rd a marked widening of the upper cardiac and aortic shadow to the right was reported and aneurism of the ascending aorta was suggested. On a second examination a change in the contour of the anterior borders of the lower thoracic vertebrae was shown by lateral films and there was now believed to be diffuse aneurism of the aortic arch. A month later, at the time of the second admission the entire chest picture had changed. The shadow which had been thought to be aneurism was larger and did not pulsate. The greatly increased opacity of the right hilus and greater part of the lower half of the right lung with slightly increased opacity of the hilus on the left now led to a diagnosis of secondary malignancy in the lungs. (See Figure 4.) Fluoroscopic examination following the oral administration of a barium meal showed a deformity of the lower third of the esophagus which was pushed forward by a large rounded mass in the posterior mediastinum, behind the shadow of the heart. The patient died on January 11th. The final diagnosis was syphilis; aneurism of the aorta with compression of the right bronchus; syphilis of the liver; probable malignancy with metastasis to the liver, lungs and mediastinum; infectious arthritis.

*Autopsy.* (A-2328.) The body was that of well developed and well nourished male negro. The abdomen was dome-shaped and more protuberant in the upper right quad-

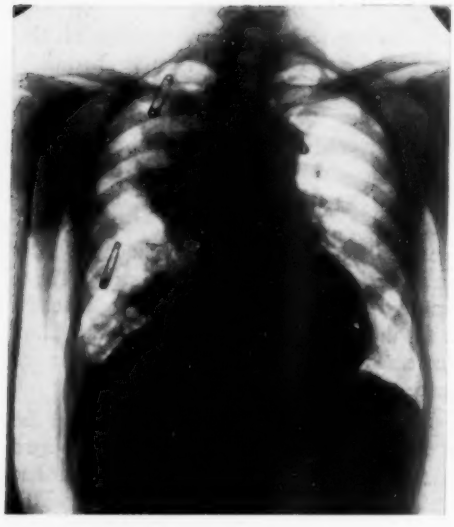

FIGURE 4. Case 9. Extensive opacity at right hilus and in lower half of right lung. Widening of upper cardiac and aortic shadow. Slightly increased opacity of hilus of left lung. At autopsy, primary carcinoma of the right main bronchus *and aneurism* of the lower thoracic aorta were found.

rant than elsewhere. Chylous fluid, about 400 cc. in amount, was found in the peritoneal cavity. Neoplasm was not found in the left lung but on the right side the main bronchus, beginning about 2 cms. below the bifurcation, was completely surrounded by neoplasm which infiltrated the wall and presented on the mucosal side as a soft, irregular elevated mass. The bronchus was much constricted at this point and also elsewhere in the secondary divisions. Surrounding the bronchi radiating extensions of the neoplasm permeated the greater part of this lung. The bronchial nodes were filled by it, the entire mass at the hilus reaching the size of a fist. In the lower portion of the thoracic aorta, just above the diaphragm, there was a large saccular aneurism, 9 cms. in diameter. This was partially filled with laminated clot anteriorly but its posterior wall was formed by the eroded bodies of the ninth and tenth thoracic vertebrae. A smaller aneurismal dilatation was found separating the muscle fibers of the diaphragm. The liver was of enormous size, measuring 32.5 by 30 by 13 cms. and weighing 5030 gms. It was filled with metastases varying in size up to that of a tangerine. Gross metastases were found also in the bronchial, mediastinal, peri-pancreatic and retro-peritoneal lymph nodes and skull.

*Pathological Diagnosis.* Primary medullary carcinoma of the right main bronchus infiltrating right lung. Multiple metastases in liver, bronchial, mediastinal, peripancreatic and retroperitoneal lymph nodes, and skull cap. Chylous ascites. Chronic purulent lobular pneumonia and bronchiectasis. Chronic organizing fibrinous pleuritis with right-sided pleural adhesions. Active syphilitic aortitis with aneurism of lower thoracic aorta, eroding bodies of ninth and tenth thoracic vertebrae. Syphilitic pancreatitis, adrenalitis and orchitis. Cardiac dilatation, more marked on right side. Fatty degenerative infiltration of heart muscle. Advanced coronary sclerosis. Marked chronic passive congestion, atrophy and parenchymatous degeneration of all organs. Marked lipoidosis of adrenals. Persistent urachus. Sub-mucosal diverticulum of bladder. Multiple adenomatous polyps of intestine. Chronic atrophic catarrhal gastro-entero-colitis. Old chronic vesiculitis and prostatitis. Old appendectomy.

*Comment.* This case offered unusual difficulty in diagnosis. A negro with syphilis complained first of pain in the feet and legs. Gradually signs and symptoms of mediastinal tumor appeared. With X-ray evidence of widening of the aortic arch, aneurism was diagnosed. The liver became of enormous size very rapidly and the upper thoracic shadow radiating in outline, so that it became necessary to include malignancy in the diagnosis. At autopsy both primary carcinoma and aortic aneurism were found. In view of the erosion of the lower thoracic vertebrae by the aneurism it is

probable that the pain in the feet and legs at the onset of the disease was due to the aneurism. That this mode of onset occurs also in cases of carcinoma of the lung without complicating aneurism is shown by other cases in this series. Since the aneurism was low in the descending thoracic aorta, the brassy cough, slight clubbing of the fingers, dyspnea and distention of the veins of the neck were due to the carcinoma. The primary growth appeared within the lumen of the right main bronchus as an irregular elevated mass. If bronchoscopic examination had been considered advisable the location and character of this new growth would have rendered its diagnosis by that method an easy matter. However, with the assumption of a probable aneurism of the aortic arch, bronchoscopy was ruled out as a method of investigation.

Clubbing of the fingers as shown by this patient and also in Cases 6 and 10 occurs frequently in carcinoma of the lung. As early as 1897 Teleky (11) had included carcinoma of the lung among the many conditions which might bring about this change.

### Case 10

#### Cough, Hemoptysis, Dyspnea, Fever, Empyema

*Clinical Abstract.* A mine laborer, 49 years old, had been well until eight months before coming to the hospital. From the beginning he had coughed and raised sputum which had been blood-flecked occasionally. About two months after the onset of his illness, fluid of unknown character was withdrawn from the left chest by the patient's home doctor. At that time the condition was thought to be tuberculosis and he was moved to the county infirmary in order not to expose his family. Cough, sputum, fever, shortness of breath and weakness persisted until entrance. There had been no pain in the chest. The left supraclavicular fossa was deep and there was flattening in the left infraclavicular region. The left side of the chest was practically immobile, and much smaller than the right when viewed from behind. The percussion note was flat over the entire left chest. The fingers showed a slight clubbing. The pupils were found to be unequal, the right being smaller than the left and the pulses were not synchronous. Aneurism or mediastinal neoplasm with effusion were considered as probable diagnoses but finally discarded in favor of chronic empyema and the patient was transferred from the Department of Internal Medicine to the Department of Surgery for rib resection and drainage. This was done and a chronic empyema found. Tissue from the thickened pleura showed inflammatory changes only. X-ray examination had shown the pleura so greatly thickened on the left as to obscure the field. The fever largely disappeared for a time after drainage was instituted but bloody purulent discharge continued and the patient began to cough up blood-stained sputum. One month after the operation there was a severe hemorrhage from the chest wound. Two months later there had been no essential change. Lipiodol injection of the trachea now showed evidence of constriction of the left main bronchus. The mediastinum was found to be displaced to the left. (See Figure 5.) The constriction was verified by bronchoscopic examination but the small tissue specimen removed at that time showed granulation tissue only. A second bronchoscopic examination was made a month later and an unsuccessful attempt to dilate the bronchial stricture, which was still believed to be of inflammatory origin, was made. Suction apparatus was used to evacuate the bronchial fistulas, apparently with effective results. The patient now complained of a greater degree of pain in the chest. He grew progressively weaker and died eight months

FIGURE 5. Case 10. Marked thickening of pleura over almost entire left field. Mediastinum displaced to the left. Lipiodol in lower right bronchial tree. (Failure of the lipiodol to enter the left main bronchus is evident in the films under strong illumination but cannot be shown clearly in reproduction because of marked density on that side.)

after entering the hospital and sixteen months after the onset of his illness.

*Autopsy.* (A-2479.) A chronic adhesive pleuritis was found on the left side, complete except for an empyema cavity containing about 200 cc. of purulent fluid. Numerous bronchiectatic cavities were found throughout the left lung. These, and the bronchi themselves, were filled with mucopurulent exudate. There was diffuse atelectasis with chronic fibroid purulent pneumonia. The secondary division of the left main bronchus leading to the lower lobe was infiltrated and practically occluded by a neoplasm which infiltrated the lung extensively and metastases of which were found in the bronchial nodes and opposite lung.

*Pathological Diagnosis.* Primary medullary carcinoma of left lung with metastases to bronchial nodes and right lung. Chronic pulmonary tuberculosis with cavitation. Chronic fibroid pneumonia. Anthracosis. Chronic adhesive pleuritis. Chronic empyema. Rib resection. Miliary tuberculosis of lungs, bronchial nodes and spleen. Acute terminal purulent broncho-pneumonia. Advanced amyloidosis of spleen (sago spleen). Early amyloidosis of kidneys and liver. General marasmus. Atrophy, chronic passive congestion and parenchymatous degeneration of all organs. Aspermatogenesis. Colloid goiter. Sclerosis of aorta and pulmonary artery. Old obliterated appendix.

*Comment.* Chronic pulmonary tuberculosis and chronic empyema concealed the primary carcinoma of the lung in this instance until autopsy. The empyema was undoubtedly secondary to the malignant disease, but was clinically considered the chief condition and repeated surgical operations were done for its relief. In spite of the utilization of bronchoscopy and radiological visualization of the bronchial tree the diagnosis was missed. The constriction of the left main bronchus was demonstrated by both methods but the tissue specimen removed was not taken from an area containing neoplastic infiltration. This biopsy showed chronic inflammatory changes only and was therefore in accord with the clinical conception of the case. The associated pyogenic process explained the low fever which continued throughout practically the entire course of the disease.

### CASE 11

### PAIN IN CHEST, PRODUCTIVE COUGH, WEAKNESS

*Clinical Abstract.* An automobile factory mechanic, age 51, entered the Department of Surgery of the University Hospital with chief complaints of weakness on exertion, pain in the chest, loss of weight and productive cough. Sixteen months before this

he had commenced to cough and raised thick white sputum. Pain in the lower right chest began four months later. Loss of appetite and 30 pounds in weight and increasing weakness were more recent developments. Non-tuberculous pleural effusion had been diagnosed outside but three attempts to tap this fluid were unsuccessful. On examination the right pupil was found to be smaller than the left, but there was a history of an old injury to the left eye which might have accounted for the difference in size. There was limited expansion on the right side of the chest and physical signs due to either effusion or consolidation with a partly or completely closed bronchus. X-ray examination revealed an area of greatly increased density in the right lower lung field, sharply demarcated above at the level of the fourth rib anteriorly. Lipiodol was successfully introduced into the left lower and right middle lobe bronchi but none entered the bronchus to the right lower lobe. (See Figure 6.) The Department of Roentgenology concurred in a diagnosis of bronchogenic carcinoma made by Internal Medicine. A low fever and leucocyte count ranging from 20,000 to 44,000 were constantly present. Thoracentesis in the sixth interspace in the right mid-axillary line yielded thick pus lying beneath a greatly thickened pleura. A rib resection was then done and a disk of thickened pleura and lung tissue removed from above a lung abscess which communicated with a medium sized bronchus. Following this operation the fever disappeared, the sputum decreased and the patient's general condition improved. On the fifth day after the operation he left his bed without permission and developed precordial pain, feeble pulse and dyspnoea. Two days later, about 17½ months after the reported onset, the patient died. Microscopical examination of the tissue removed at operation showed medullary carcinoma lining a part of the cavity. The final diagnosis was primary carcinoma of the right lower lobe of the lung with secondary abscess formation.

*Autopsy.* (A-2776.) The recent thoracotomy wound in the right axilla was filled with a light gauze pack which was soaked with pus. Except for this area the right pleural cavity was almost entirely obliterated by adhesions. The left pleural cavity was free from adhesions and there was no fluid. The pericardium was covered with fibrinous exudate. Section of the left lung showed no neoplasm. On opening the main bronchus to the right lung it was found to be surrounded by a neoplastic mass beginning at a point 2 cms. below the bifurcation of the trachea, and extending particularly into the lower lobe. At a point 5 cms. below the bifurcation the bronchus showed complete stenosis. The growth spread radially from this point toward the base and laterally and formed a portion of the wall of the cavity which had been opened surgically.

FIGURE 6. Case 11. Greatly increased density in lower right lung field. Lipiodol successfully introduced into the left lower and right middle lobe bronchi, but not into the bronchus of the right lower lobe. Primary squamous cell carcinoma of right main bronchus.

*Pathological Diagnosis.* Primary non-cornifying medullary squamous cell carcinoma of the right main bronchus, infiltrating mediastinum, lung and pericardium. Metas-

tases to right lung, bronchial and retroperitoneal lymph nodes. Chronic purulent fibroid pneumonia in lower right lung peripheral to neoplastic bronchial stenosis. Atelectasis and emphysema. Chronic abscess of lower right lobe (drainage of lung abscess seven days before death). Subacute fibrinopurulent pericarditis. Right-sided chronic adhesive pleuritis. Chronic atrophic catarrhal gastro-entero-colitis. Chronic leptomeningitis. Right-sided cardiac dilatation. Acute exacerbation of chronic passive congestion and atrophy of all organs.

*Comment.* In view of the fact that the primary carcinoma was on the right side the smaller size of the right pupil as compared to the left was probably significant and not due to the old trauma. The pain in the chest accurately indicated the primary site in this instance. The secondary pyogenic infection with abscess formation, peripheral to the constricted bronchus, confused the diagnosis somewhat by giving a leucocytosis and fever. Extension of the infection to the pericardial sac directly or by metastasis must have taken place before the operation for the exudate showed considerable organization. This would assist in explaining the leucocytosis which reached 44,000 on one occasion.

### Case 12

### Pain in Lower Back and Legs

*Clinical Abstract.* A sheet metal worker, 50 years old, was admitted to the Surgery Department of the University Hospital complaining of pain in both legs and lower back. He believed that his trouble began with a slight injury to the foot nine months before. This injury was of minor consequence but the pain in his back and legs continued, radiating from the lumbosacral region down to the posterior aspect of both legs. His right leg had become functionless, apparently because of pain. The patient stated that he had lost 60 or 70 pounds since the onset of his illness. There was marked tenderness of the lumbosacral region and the patient could be turned from side to side only with the greatest difficulty because of the pain occasioned by any movement of the lower back. Routine physical examinations of the chest and abdomen were negative. X-ray studies of lumbosacral spine and both hips showed definite changes in density which were thought to be suggestive of metastatic carcinoma. The prostate was examined on several occasions and was negative except for a slight increase in size. A barium enema showed good filling of the colon with no evidence of pathology. A provisional diagnosis of sarcoma of the sacrum was made. The patient was given several X-ray treatments over the pelvis both anteriorly and posteriorly with slight temporary relief from his pain. He died four months after admission and about 13 months after the reputed onset of his disease.

*Autopsy.* (A-2818.) Externally, the right thigh was found to be edematous and enlarged, particularly in the upper third. At the root of the left lung a firm neoplastic mass, about 3 cms. in diameter, was located. This was in relationship to the left main bronchus and at a point 2.5 cms. below the tracheal bifurcation the neoplasm appeared within the bronchial wall, infiltrating the mucosa. Section of the left lung showed that the neoplasm had spread in a fan-shaped manner from the hilus, reaching practically to the apex where the largest of the masses within the substance of the lung was found. The base of the heart was involved by direct extension. The lower vertebrae, sacrum, pelvic bones and upper end of the right femur were filled with neoplasm metastases and were so nearly completely destroyed that they could be cut with a knife.

*Pathological Diagnosis.* Primary medullary small-celled carcinoma of left main bronchus. Extension into pericardium. Metastases in left lung, liver, pancreas, prevertebral lymph nodes, lumbar vertebrae, ilium, pubis and right femur. Emphysema,

congestion and edema of lungs. Marked atrophy of heart. Subepicardial fatty infiltration. Myocardial fibrosis. Advanced coronary sclerosis. Atherosclerosis of aorta. Chronic passive congestion, atrophy and parenchymatous degeneration of all organs. Chronic pyelonephritis with old healed tubular nephritis. Chronic cystitis. Chronic catarrhal gastritis. Chronic interstitial pancreatitis. Marked lipoidosis of adrenals. Complete fibroid atrophy of testes. Thrombosis of spermatic vessels. Thrombosis of prostatic plexus extending into iliac vein and inferior vena cava. Edema of right leg and scrotum.

*Comment.* Again we have a patient whose entire clinical history is occupied by one of the distant effects of primary carcinoma of the lung—pain in the legs from metastatic involvement of the lower vertebrae, pelvic bones and adjacent soft parts. The innumerable bone metastases had produced such marked changes that primary sarcoma of the sacrum was the working diagnosis. It is unfortunate that X-ray study of the lungs was not undertaken. If this had been done a correct diagnosis should have been made for the areas of increased density would have been found to have a distribution quite unlike that of hematogenous metastases of sarcoma in the lung.

When the outstanding signs and symptoms in this series of twelve cases of primary carcinoma of the lungs and bronchi are tabulated the list closely resembles that given in the introductory paragraph. The outstanding signs and symptoms and the number of time each was encountered were as follows: Cough, 5; dyspnoea, 4; loss of weight, 4; pain in chest, 3; hemoptysis, 3; pupillary changes, 3; oedema and congestion of upper half of body, 3; clubbing of fingers, 3; pain in back, 3; pain in legs, 3; extension through thoracic wall, 3; recurrent laryngeal paralysis, 2; pleural effusion, 2; weakness, 2; abdominal pain, 2; metastases in cervical nodes, 2; dysphagia, 2; fever, 2; cyanosis, 1; pain in arms, 1; sputum without blood, 1; vomiting, 1; pulses not synchronous at wrists, 1; drooping of eyelid, 1; coma, 1; paralysis of lower extremities, 1. The most noticeable omission from our series of cases is that of one illustrative of those which enter neuropsychiatric clinics because of changes dependent upon metastases to the brain and meninges. These form a large group in the literature but through chance assortment are not represented in our series.

The list given above does not include a new sign or symptom and it does not include one which is pathognostic of primary carcinoma of the lungs. By the very nature of the condition it becomes highly improbable that such a sign will ever be found. It is hoped, however, that by the presentation of this series of microscopically verified cases after the manner of a clinical-pathological conference—a dry clinic, if you wish—the types of cases in which carcinoma of the lung should be considered have been emphasized.

Senior medical students sometimes ask why so much effort is made to diagnose carcinoma of the lung when so little can be done about it therapeutically once the diagnosis has been established. To most of us the satisfaction experienced in arriving at a

correct solution of a puzzling clinical or pathological problem is answer enough. However, the advantages to the patient may be considerable even in the absence of therapy. Some of these cases spend much time away from friends and family and are at a considerable expenditure of money while laboring under a diagnosis of tuberculosis. Any large tuberculosis sanatorium harbors cases of primary carcinoma of the lung from time to time. Two of our series were thus treated. Others, like our Case 2, are required to submit to unnecessary laparotomy. Finally, if any progress is to be made in the surgical handling of primary carcinoma of the lungs and bronchi the medical profession must learn to recognize this condition very much earlier in the course of the disease than is done at the present time. Certain cases in which the early growth is papillomatous and endobronchial are entirely suitable for removal through the bronchoscope (3), while in other cases early carcinoma well out in the parenchyma may be removed by partial lobectomy. Brunn (12) found that there are reports of at least 28 instances of surgical intervention for this condition in the literature. Perhaps the stage at which carcinoma of the lung is diagnosed has already been moved back from the autopsy room to the last few months of life. It must be set back by a very much greater interval if there is to be any chance for successful intervention.

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# The Blood as a Diagnostic Aid in the Differential Diagnosis of the Lymphadenopathies*

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IN any discussion of the blood as a diagnostic aid must come a reiteration of the now generally accepted belief that changes in the blood do not constitute a disease but are merely manifestations of what is taking place in the blood forming organs. Vogel (1) has called attention to this in an excellent analogy between the blood as a secretion, and the gastric juice. The absurdity of calling hyperchlorhydria a disease of the gastric juice makes any consideration of "diseases of the blood," as such, untenable. Piney (2) says:

> "To-day we have had to give up the older conception of the blood as a special form of connective tissue with a fluid matrix; we have to regard it as a composite containing the products of all the hematopoietic tissues."

We pass on then to a consideration of the lymphadenopathies with a better idea, perhaps, of what not to expect in the way of constancy of changes in the blood in these complex conditions. Moreover, in the absence of any histological differentiation in lymphosarcoma, leukemia and pseudo-leukemia, one wonders (and that in conjunction with many others) whether these are not all the same disease in various expressions or exhibitions of reaction to the same underlying cause. Typhoid fever, for example, may express itself in many ways, occasionally with mental symptoms predominating, sometimes respiratory, sometimes abdominal, at other times renal. Why is it not logical to expect, particularly in view of the similar histology that lymphosarcoma, leukemia and pseudo-leukemia are analogous expressions of some disease process, with the blood picture only one symptom of the clinical syndrome? The leukosarcomata may furnish the clue to bridge the gap, exhibiting a lymphosarcomatous type of tumor pathologically, terminating with the picture of an acute leukemia.

In differentiating the group of lymphadenopathies, we fall back at once to weed out one member on a purely pathological basis. Biopsy, at present, enables a definite diagnosis in the great majority of cases in Hodgkin's disease only. The very early stage of lymphoid hyperplasia is, of course, not pathognomonic, but the later

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picture of proliferation of the reticulo-endothelial cells, giant cells and eosinophiles, stamps this disease in unmistakable fashion. Histologically, lymphosarcoma, leukemia and pseudo-leukemia have nothing to differentiate them. The term "pseudo-leukemia" requires definition, as this nomenclature has been used at different times to designate more than one condition. We shall defer this definition, however, until pseudo-leukemia itself is taken up later in the course of this paper.

Clinically, the differential diagnosis of enlargement of the lymph nodes is not readily made. In recent years further to complicate the clinical picture, have come the recognition and renewed studies of infectious mononucleosis (glandular fever, acute benign lymphoblastosis). Its very close resemblance to the leukemias has given rise to grave doubts in the diagnosis in many instances. The literature abounds in reports of cases which, because of blood cell changes and clinical findings, have been thought to be leukemia.

It is our purpose to point out the diagnostic aids to be derived from a study of the blood in the lymphadenopathies. We shall begin with the closest simulator of leukemia, namely infectious mononucleosis.

## Infectious Mononucleosis (Glandular Fever)

Observers (3, 4, 5) are agreed that there is almost always a lymphocytosis and moderate increase in the total number of white blood cells, together with a blood picture which might be confused with acute leukemia. Longcope (6) remarks the very striking resemblance to leukemia, but hastens to point out that the clinical picture,

> "early and marked enlargement of the lymph nodes, the absence of anemia and of purpura," and "the histological and biological character of the abnormal mononuclear elements of the blood, practically exclude the possibility of considering these cases as instances of mild and transient leukemia."

The classification of the type or types of cell met with is difficult. Downey and McKinlay (7) have described three separate types. They add:

> "nearly all of the lymphoid cells of the blood, when first examined, were atypical to the extent illustrated in the figures. The size and form of the nucleus are of little value in determining genetic relationships or stages of differentiation of the cells, but the quantity and distribution of chromatin and its relation to the parachromatin is of great importance."

Baldridge (8) and his co-workers report variation in the blood findings. Leucocytosis of varying degree was present sometime during the course, in most cases. In most instances, cases with marked temperature reactions showed a leucocytosis with relative polymorphonuclear increase during the course, particularly while temperature persisted. The largest total leucocyte count was 26,950. "Most of the cases which were followed developed a leukopenia at some time during their course, usually in from two to four weeks after the onset." The lowest count was 3,400.

The average of 136 counts on 50 patients, as given by them, are as follows:

| W.B.C. | Polys. | Monos. | Eos. | Baso. | R.B.C. | HGB. |
|---|---|---|---|---|---|---|
| 10,177 | 48.4 | 50.2 | 1.1 | 0.2 | 2,800,000 | 92.2 |

Their summary of noteworthy blood findings is:

1. Leukocytosis sometime during the course of the disease, usually at the onset and as a rule not above 20,000.
2. During convalescence total white count below average normal frequently met with.
3. Percentage of mononuclears appears to average higher in sporadic than in epidemic cases.
4. Degree of fever and polynuclear increase appear related.
5. Mononucleosis develops as the fever subsides.

Cotrell (9) recently studied 12 cases of infectious mononucleosis and observed:

1. "An increase in the lymphocytes amounting to 40 per cent or more of the total leukocytosis."
2. "Increase in the total number of leukocytosis."

## Character of the Mononuclear Cells

The mononuclears, although abnormal, differ from the cells seen in lymphatic leukemia. Bloedorn and Haughton (5) point out that these cells do not show the "poor staining reaction of the cytoplasm and nucleus" seen in leukemia. Furthermore, no degenerated cells were seen in their series of acute benign lymphoblastosis cases, such as are frequently met with in the acute leukemias. They add:

> "The heavy staining nuclei of the lymphoblast in this disease may be placed centrally or eccentrically; it is often round, oval or irregular in outline, showing deep indentations and occasionally showing the clover leaf or bilobed Rieder type nucleus. Occasionally, azure granules were noted in the cytoplasm and vacuoles in the dark opaque blue were not infrequently noted. None of these cells showed an oxidase ferment, thus differing from those of myelocytic origin.
>
> "The small lymphocyte, as a rule, stained normally with Wright's stain, but the majority of cells making up this group consist of large lymphadenoid cells with a protoplasm so darkly stained that it is at first difficult to distinguish them from myelocytes."

Weil (10) has called these cells "non-granular myelocytes" and described them as follows:

> "They look like a myelocyte whose granules have fused into a smooth homogenous band of color around the spherical or ovoid nucleus. The protoplasm is homogeneous and deeply stained."

Morse (11) notes that the blood smear is different from that in leukemia. There is an absence of "immature, atypical and degenerating forms of leukocytes and the presence of large numbers of the bilobed or Rieder type of white cell is quite distinctive."

Baldridge (8) and his co-workers have described the abnormal cells as follows:

> "The size varies from but little larger than the small lymphocyte to cells as large or even larger than the largest cells of normal blood. The inner structure of the nucleus in some is like that of the normal lymphocyte in that it is made up of irregular bands of chromatin which give it a rather wavy appearance.
>
> "Nucleoli are not at all common. Occasionally nuclei are met with in which there is a very marked condensation of chromatin near the periphery giving a suggestion of the clock-faced appearance

seen in plasma cells. The chromatin arrangement within the nuclei of many of the cells in our series was very close to that seen in normal monocytes.

"The cytoplasm of the cells varies somewhat in amount but is usually more abundant than in the normal lymphocyte. Stained with modifications of the Romanowski method there is a great variation in the number and size of azurophil granules."

Downey and McKinlay (7) warn that the "finding of an occasional immature cell does not warrant the diagnosis of acute leukemia even though the clinical picture is suggestive."

Sprunt and Evans (3) discuss the difficulty in differential diagnosis from a beginning lymphatic leukemia. The more marked anemia, tendency to hemorrhage and fragility of the cells with the production of "smudges" in the blood smear, point to an acute leukemia. The blood picture in infectious mononucleosis, according to them, shows usually a normal or only slightly increased leukocyte count in the first few days, followed by a leucocytosis of 13,000 to 20,000 per cmm., with an increase in percentage of mononuclears.

*Comment*: On the basis of this review, it would seem that there is still difference of opinion as to the practicability of diagnosis of infectious mononucleosis on the blood smear alone. The border-line cases, with clinical manifestations suggestive of acute leukemia, are most difficult.

In contrast to Downey and McKinlay's (7) observations that

"In every case it was possible to determine the non-leukemic value of the blood, even though the clinical picture suggested acute leukemia."

others (Sprunt and Evans (3) and Schenck and Perry Pepper (12)) are not so optimistic. The latter authors write:

"Some believe that the differential diagnosis can be made from a careful study of the predominating type of cell but this is very difficult."

Baldridge and his co-workers (8) believe that:

"While certain individual blood cells may be found in glandular fever which resemble the very unripe elements of acute leukemia—in our experience a differential study of 100 cells has been ample to establish the diagnosis."

Bloedorn and Haughton (5) remark:

"Nevertheless the resemblance to leukemia has been so striking in some of the cases that eminent hematologists have considered it impossible to differentiate this condition on the blood smears alone."

Schenck and Perry Pepper (12) observe:

"It is quite possible to believe that, certainly on the blood picture alone, it would be impossible to differentiate between certain cases of infectious mononucleosis and acute leukemia."

When such difference of opinion exists where shall the fact be found? If we assume with some that the diagnosis in every case can be made on the blood smear alone, how shall we account for those cases where competent observers have been at a loss to differentiate the blood smear from that of a leukemia? The answer lies, we believe, in the personal equation, a variable entity to be sure, but always with us and indispensable to the bulk of thought that lies at the foundation of medical knowledge. When

some are anxious to lead along paths that most others are not ready to follow, is it not wisest for us to pause and look longer before we go on?

### Hodgkin's Disease

From the many studies on the blood made in this condition, the conclusion is warranted that there is little specific in the blood picture. A secondary anemia is commonly present, although the red blood cells are not usually greatly reduced. Naegeli (13) notes the hemoglobin seldom under 60-80 per cent. In a few cases, severe anemia has been noted: Frankel and Much (14)—1,140,000; Hirschfeldt (15) 1,000,000 with hemoglobin of 20 per cent. On the other hand, where much cyanosis and dyspnoea are present as a result of compression, high red counts and hemoglobin have been reported (Naegeli (13)) up to 6,000,000 and HB. 125.

Sir Humphrey Rolleston (16) observes:

> "The white count does not show any constant or characteristic change. Usually leukocytosis is absent and there may be a leukopenia with a relative lymphocyte increase, especially, I believe, when the spleen is predominantly affected, a view shared by Weber (17)."

Naegeli (13) notes leukopenia particularly in the abdominal forms of the disease.

Various observers have called attention to certain phases they deemed characteristic, but these findings have, on the whole, not been demonstrated consistently enough to warrant their designation as typical of this disease. Bunting (18) believed that the most striking feature of the white blood cell count was a high percentage of transitional leukocytes in all stages, due possibly he suggested, to the proliferation of the endothelial cells of the lymph nodes. Though he believed the findings to be of diagnostic value, others (Perry Pepper (45)) have questioned their importance.

The latter author says:

> "A relative or even an actual increase in the mononuclear and transitional cells seems to be the most constant finding but this is far from being pathognomonic of Hodgkin's disease."

Steiger (26) thinks that the differential leukocyte count is characteristic of the stage of the disease, namely: a lymphocytosis in the early stage of lymphoid hyperplasia; a neutrophilia in the second stage; and, finally, a lymphopenia in the last stage with onset of fibrosis. It is very doubtful, however, that such a rigid grouping can be made. It is pointed out that it is usual for the disease to be present in different stages in different lymph nodes and therefore unlikely that a clear cut blood picture should be present at any time, assuming the basis of the differentiation to be true.

In a later study, Bunting (46) noted the absence of a single constant blood picture in Hodgkin's. He believes, however, that two groups of cases can be distinguished:

1. Those of a duration of one year or less.
   A. Normal or somewhat increased leukocyte count and a normal or slightly decreased percentage of polymorphonuclears.
2. Cases of more than one year's duration.
   A. Sharp leukocytosis
   B. High percentage of polymorphonuclears.

and throughout the disease

1. An increase of transitional leukocytes.
2. A gradual decrease in the lymphocytes.

Piney (2) (page 142) remarks that: "leukocytosis is almost invariable and there is no other disease (in which clinical evidence of infection is absent) in which a very high number of leukocytes can persist for so long a time."

Naegeli (13) makes a similar observation as to the persistent leukocytosis, reporting six cases from personal observation, with counts of 41,000, 45,000, 46,000, 48,000, 50,000 and 55,400.

*Comment*: In brief, then, although many conditions of interest in the blood picture have been observed in Hodgkin's disease from time to time, looking at the broad vista of accumulated evidence we are led to agree with Piney's (2) remark that: "the blood changes in Hodgkin's disease are far from spectacular . . . ."

## Pseudo-Leukemia

Much difference of opinion exists as to the correctness or advisability of retaining this nomenclature which was first used by Cohnheim (27) in describing a condition presenting anatomical characteristics similar to the leukemias previously described by Virchow (28), but having no changes in the blood. Naegeli (13) uses the term to denote a "symptom-complex" and not a disease, denoting, by pseudo-leukemia, conditions resembling the external appearance of leukemia (enlargement of the lymph nodes and spleen), but lacking the blood changes of leukemia.

Jagic (29) says:

"From a clinical standpoint we can dispense with the term 'pseudo-leukemia' because in the majority of instances we are able to make a clinical diagnosis which corresponds to the recognized anatomical picture."

As used here, the term "pseudo-leukemia" is not related to aleukemic leukemia. By the latter term we mean to denote that stage of a true leukemia in which the blood picture does not show the high leucocyte count typical of the disease, although the differential count is almost always suggestive.

In using the term "pseudo-leukemia" we refer particularly to that condition which some observers believe is an entity, both from the clinical and anatomical standpoint. We have no reference here to the so-called aleukemic phase of leukemia. Symmers (47), for example, out of a large experience with diseases of the lymphoid apparatus, points out its anatomical and clinical characteristics, particularly with reference to its clinical resemblance to leukemia, Hodgkin's disease, lymphosarcoma, and the like, and its gastro-intestinal manifestations, which are sometimes extraordinarily extensive. This observer's definition of the disease concurs with that of Cohnheim (27); they agree that it is a disease with all the anatomical characteristics of chronic lymphatic leukemia, without changes in the blood.

Pseudo-leukemia presents no blood changes to differentiate it from lymphosarcoma, nor is there any histologic difference demonstrable in the lymph nodes or elsewhere. Pseudo-leukemia, according to Symmers (30),

"produces no destructive infiltration of tissues but limits its activities to the lymphoid structures, and the spleen is almost invariably enlarged, whereas the opposite is not unusual in lymphosarcoma."

The blood count given in one of Symmers' (48) cases of pseudo-leukemia was:

| WBC | Polys. | Small Lymphs | Large Lymphs | Eos. | Baso. | RBC | HB. |
|---|---|---|---|---|---|---|---|
| 11,000 | 72 | 24 | 3 | 1 | .. | 5,240,000 | 80 |

In cases previously reported in the literature, there is no outstanding feature in the blood examination, only slight leukocytosis being reported—11,800 by Carrington (31) and 10,600 by Celler (32).

### Leukosarcoma

Sternberg (33) used the term leukosarcoma to denote a group of cases characterized by a leukemic blood picture and an invasive lymphoid tumor. That this condition is an entity unrelated to leukemia is not believed by most observers. Turk (34) and Naegeli (13) consider leukosarcoma as only a stage of lymphatic leukemia.

When the case is fully established, the leukemic blood picture present resembles, in most respects, that found in acute leukemia. There is a hign percentage of large lymphoid or so-called "leukosarcoma" cells. Small lymphcocytes are not predominant.

Early in the disease the leukemic blood picture may not be manifest, the symptoms at such time being referable solely to the presence of the invasive tumor, most often of mediastinal origin.

In connection with this location of the tumor growth, it is of interest to note, as Symmers (30) points out, "the astounding, if ominous fact, that in these circumstances the changes enumerated may stretch themselves over an extended period without eliciting any complaint from the patient and both subjective and objective disturbances may be registered suddenly and without warning at a time when anatomic expansion has advanced beyond all hope of control."

Webster (35) gives the following counts in cases of leukosarcoma, in various phases:

| | W.B.C. | Polys. | Small Monos. | Eosin. | Trans. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|
| Case 1. | 33,000 | 21.8 | 76.0 | 0.8 | 6.0 | 5,220,000 | 85% |
| | 4,000 | 74. | 21. | 2.8 | 0.4 | 4,588,000 | .. |
| Case 2. | 230,500 | (Differential not given. Small lymphocytes predominant) | | | | | |
| Case 3. | 3,960 | 60. | 32. | .. | 8. | ..... | .. |
| | 87,400 | 0 | 43. | Smudges 57% | | | |

Sternberg's (35) case, about ten days before death, showed:

| W.B.C. | Polys. | Lymphs. | Large Monos. | Myelocytes |
|---|---|---|---|---|
| 6,800 | 5 | 6 | 85 | 4 |

### Lymphosarcoma

When Kundrat (36) first described the condition now known as lymphosarcoma, namely a diffuse proliferation in lymphoid structures of lymphocytes in an inconspicuous stroma, he propounded as a characteristic of the growth its tendency to remain confined within sharp limits. He noted, however, its capacity to invade locally and often extensively. Symmers (30) very recently has reported a study of 17 cases, 9 of which, as the author states, "fulfill faithfully Kundrat's maxim of local growth"; the other 8 "have brought about a degree of territorial expansion seldom distanced by any of the other diseases of the lymphoid apparatus." It is important to note this writer's observation of the many clinical similarities between Hodgkin's disease and lymphosarcoma and even in the early stages, of the histological resemblances, when the picture in both shows a simple, diffuse hyperplasia of the lymphoid cells. In none of his cases was there anything typical in the blood picture, the two cases terminating with a blood picture of acute leukemia coming under the classification of what has been described as leukosarcomatosis.

There is nothing characteristic in the blood picture of any type of lymphosarcoma; anemia is often absent. Nægeli (13) notes a reduction of the lymphocytes, recording the following counts:

| W.B.C. | Lymphs. |
|---|---|
| 6,000 | 33% |
| 5,000 | 18 |
| 7,000 | 15 |
| 10,400 | 7 |
| 8,600 | 15 |
| 7,200 | 27 large lymphs. |
| 21,600 | 2 |
| 6,800 | 19 |
| 4,600 | 16 |
| 11,460 | 6 |
| 41,500 | 6 (case had metastasis to skin and bone marrow) |

Pathologic forms of lymphocytes have not been observed in lymphosarcoma, occasionally large lymphocytes were noticed but no lymphoblasts.

This author notes that the diagnosis of the condition in progressive cases is usually not difficult, particularly in the mediastinal ones, being, as they are, made on general clinical observation and not on blood findings. There may be a moderate leucocytosis, but there is nothing unusual in the differential count.

### Leukemia

To discuss the blood findings and variations possible in the different types of leukemia, acute and chronic, with their subdivisions, is far beyond the province of this paper. Some pertinent facts, however, must be alluded to. The temporary resemblance to leukemia of the blood picture in some cases of infectious mononucleosis has already been pointed out. The suggestive relationship of leukosarcoma and lymphosarcoma to the leukemias has been referred to.

Some general remarks on the blood in leukemia are of interest. DiGug-

lielmo (37) notes that the "more acute the leukemic process the less mature and differentiated appear the cellular forms which are carried from the place of their original location into the blood stream."

In the most acute form of leukemia he observed the predominance of hemocytoblasts; in the less rapid type, the more differentiated elements appear (myeloblasts in the myeloid type; lymphoblasts in the lymphatic type) and in chronic cases the number of granular cells, lymphocytes and monocytes are greatly increased.

What interests us particularly are those types of leukemia frequently referred to as aleukemic leukemia. By this term we mean to denote, as previously pointed out, those cases proved at some time to be true leukemia, but which, at the particular time the case comes under observation, show a normal or decreased total white count. This type of case offers a difficult problem, at times, in differential diagnosis.

Naish and Tingle (38) reported a case of leukemia with a complete absence of any, even temporary, leukocytosis, showing a low total number of polymorphonuclears with a stability of the leukocyte count over a long period. The count, on one occasion was:

| W.B.C. | Polys. | Small Monos. | Large Monos. | R.B.C. |
|---|---|---|---|---|
| 2,900 | 25 | 13 | 62 | 850,000 |

Autopsy showed leukemic infiltration of the liver and spleen.

Fox and Farley (39) report two cases of aleukemic leukemia, one of which was an undoubted case and proven at autopsy; the other case did not come to autopsy but the biopsy excluded Hodgkin's disease.
They note:

> "The two cases of aleukemic leukemia reported, while showing extensive involvement of the lymphatic apparatus, gave no reduction of circulatory mononuclears, a relative reduction being a picture usually seen in granulomata and sarcomata, involving much of the lymphatic apparatus. This point should be a decided help in clinical differential diagnosis."

Jaffee (40) finds that "normal or subnormal leukocyte counts in typical myelogenous leukemia are far from rare." He reports two cases of aleukemic myelosis (the aleukemic form of myelogenous leukemia) in which "the excessive proliferation of the myeloid tissue—caused no characteristic change of the blood picture and the true nature of the disease was revealed only by the histologic study of the organs involved." In true aleukemic myelosis, he adds, the white blood picture remains normal, giving no information as to the extensive proliferation of the myeloid tissue.

Brill (41) discussing aleukemic leukemia, notes that "a careful examination of the blood, however, usually shows abnormal white cells par-

| | W.B.C. | Polys. | Lymph. | Mono. | Trans. | Eos. | Baso. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|---|---|
| Case 1. | 5,900 | 54 | 38 | 6 | 1 | 4 | .. | 4,670,000 | 88 |
| (Autopsy) | 6,500 | 52 | 40 | 3 | 3 | 1 | 1 | 5,400,000 | 93 |
| Case 2. | 13,800 | 43 | 36 | 11 | 7 | 3 | .. | 4,800,000 | 82 |
| | 28,000 | 77 | 16 | 6 | 1 | .. | .. | 4,810,000 | .. |

ticularly characterized by qualitative changes . . . ."

*Comment*: Doubtless, much more might be said about rare types of leukemias. It is sufficient for our purpose, however to call attention to some of these problems as relating to the leukemias and to point out that at times confirmation of the diagnosis leukemia may be lacking in the examination of the blood.

### Follicular Lymphadenopathy with Splenomegaly

Very recently there has been described (42, 49) a condition, perhaps first noted by Becker (43), of generalized enlargement of the lymph nodes with splenomegaly. The nodes involved may be superficial or deep or both. Histologically, as Symmers (49) observes, the picture is characterized "almost exclusively by numerical and dimensional hyperplasia of the germinal follicles." Clinically, it presents essentially gross identical features with Hodgkin's granuloma, chronic lymphatic leukemia, pseudo-leukemia and lymphosarcoma, except that, even if untreated, it does not menace life.

Thus far, if Becker's (43) case be included, only six cases have been reported. The lesion appears to be definitely and favorably affected by the X-ray.

There is nothing characteristic in the blood, biopsy, only, enabling the establishment of the diagnosis.

The fact that this condition is benign sheds the first ray of hope on this group of lymphadenopathies which, aside from infectious mononucleosis, have led to a uniformly fatal termination.

### Tuberculous Lymphadenitis

Although the process is most often localized, there are some cases in which widespread involvement occurs, closely resembling the external anatomical characteristics of Hodgkin's disease and the leukemias. Biopsy, of course, at once makes the diagnosis clear, but from the standpoint of the blood alone there is nothing specific in the hematologic picture.

Nægeli (13) notes a marked reduction in the leukocytes in most cases, calling attention, however, to the occurrence of a moderate leukocytosis in some instances. In connection with the low white count usually present in tuberculosis, he warns of that phase of leukemia in which the white count is relatively normal or even lower. In one of his cases of generalized lymph node tuberculosis, shown in all the nodes histologically at autopsy, there was a leukopenia of 2-3-4,000 (numerous counts in two years) with a reduction of the lymphocytes (300-500 per cmm.)

Bäumler (50) reported similar low counts in his case, and Fabian (quoted by Nægeli (13)) reported a case with a count of 3,800 white blood cells, with 92 per cent polymorphonuclears and only 5 per cent lymphocytes.

Severe anemia, according to Fleischmann (51), seldom occurs in generalized tuberculous granuloma, but Nægeli (13) was able to demonstrate polychromatophilia and basophilic stippling even when anemia was absent.

In a general way, according to the latter author, from the standpoint of

differential diagnosis a leukopenia is against Hodgkin's disease and for tuberculosis, whereas a distinct leukocytosis is strongly in favor of Hodgkin's and has as yet never been found in diffuse tuberculous lymph granuloma.

## Summary

The writers have attempted, by a study of the pertinent literature, to point out the diagnostic aids to be derived from examination of the blood in Hodgkin's disease, lymphosarcoma, leukosarcoma, pseudo-leukemia, leukemia, follicular lymphadenopathy with splenomegaly and tuberculous lymphadenitis. They wish to acknowledge that in many cases they have drawn freely from the writing of those quoted.

On the whole, up to the present time, there is no specific blood picture in Hodgkin's disease, in the so-called pseudo-leukemia of Cohnheim, in lymphosarcoma, leukosarcoma, in the benign follicular lymphadenopathy with splenomegaly or in tuberculous lymphadenitis. Some characteristics (increase in transitional leukocytes, particularly) have been pointed out for Hodgkin's disease, but their value is questionable from a diagnostic standpoint. The chief difficulty, at present, lies in the differential diagnosis between infectious mononucleosis and the aleukemic stage of lymphatic leukemia. Difference of opinion as to the solution of this problem on the blood findings alone still exists among competent observers.

If we have shed no new light on the problems of the lymphadenopathies, we trust that we have illuminated those already explored realms now resting, perhaps, too comfortably in the shadow of the great heap of accumulated data.

Table I—Blood Counts in Infectious Mononucleosis
(Downey & McKinlay (7))

| Case | Date | W.B.C. | Polys. | Lymph. | Lymphs. Sm. | Lymphs. Lge. | Tr. | L.M. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. | 3/ 6/21 | 3,000 | .. | .. | .. | .. | .. | .. | ..... | .. |
| | 3/12/21 | 17,200 | 20 | 80 | .. | .. | .. | .. | 3,904,000 | |
| | 11/ 3/21 | 7,000 | 56 | | 8 | 37 | 4 | .. | | |
| | 2/24/22 | 7,150 | 55 | | 21 | 17 | 4 | 3 | | |
| | 6/ 8/22 | | 71 | | 29 | | | | | |
| 2. | 11/ 3/21 | 16,100 | 21 | | 8 | 67 | 4 | .. | 6,400,000 | 85% |
| 3. | 3/ 8/22 | 26,200 | 25 | 74 | | | .. | 1 | 5,184,000 | 90 |
| | 6/ 1/22 | 7,000 | 38 | 57 | | | .. | 5 | 4,992,000 | 85 |
| 4. | 4/10/22 | 26,000 | 18 | 77 | | | 1 | 4 | 4,416,000 | 75 |
| | 6/ 5/22 | 8,400 | 46 | 45 | | | 4 | 5 | 4,416,000 | 80 |
| 5. | 5/ 9/22 | 11,600 | 32 | 56 | | | 6 | 6 | 4,224,000 | 80 |
| 6. | 12/15/21 | 10,700 | 41 | | 40 | 15 | 1 | 3 | ..... | .. |
| 7. | 8/15/22 | 12,800 | 13 | 77 | | | 4 | 6 | 4,042,000 | 70 |
| 8. | 9/26/22 | 15,000 | 43 | 57 | | | .. | .. | ..... | 85 |
| 9. | 10/30/22 | 11,750 | 56 | | 23 | 13 | 5 | 3 | | |
| | 11/ 7/22 | 5,850 | 42 | | 46 | 6 | 4 | .. | ..... | .. |

TABLE II—BLOOD COUNTS IN INFECTIOUS MONONUCLEOSIS
(Bloedorn, W. A. & Haughton, J. E. (5))

| Case | Date | W.B.C. | Poly. | Lym. | Mono. | Tr. | Eos. | Mast Cell | Myel. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. | 3/18/20 | 30,000 | 15 | 84 | .. | .. | .. | .. | 1 | 4,200,000 | 78% |
| | 12/ 2/20 | 7,100 | 57 | 39 | 0.5 | 0.5 | 2.0 | 1. | .. | 5,400,000 | 100 |
| 2. | 10/18/20 | 9,100 | 26 | 71 | 1. | 2. | .. | .. | .. | 4,700,000 | 90 |
| | 12/ 1/20 | 7,000 | 71 | 25 | 2. | 0.5 | 0.5 | .. | .. | 5,200,000 | 100 |
| 3. | 11/ 2/20 | 20,100 | 24 | 74 | .. | .. | .. | 1. | .. | ..... | .. |
| | 12/ 2/20 | 7,000 | 38 | 54.5 | 2. | 3. | 3. | 0.5 | .. | 4,600,000 | 95 |
| 4. | 12/ 6/20 | 6,000 | 46 | 51 | .. | 2. | .. | 0.5 | .. | ..... | .. |
| | 12/ 6/20 | 7,200 | 53 | 39 | 2. | 1.5 | 1.5 | 2. | .. | 5,330,000 | 100 |

TABLE III—BLOOD COUNTS IN INFECTIOUS MONONUCLEOSIS (GLANDULAR FEVER)
(Baldridge, et al. (8))

| Case | Date | W.B.C. | Polys. | Monos. | Eos. | Baso. |
|---|---|---|---|---|---|---|
| 1. | 5/27/18 | 14,200 | 15 | 85 | .. | .. |
| | 6/11/18 | 3,600 | 36 | 64 | .. | .. |
| | 6/25/18 | 5,800 | 60 | 38 | .. | 2 |
| | 6/31/18 | 13,400 | 41 | 59 | .. | .. |
| 2. | 4/29/24 | 15,150 | 69 | 31 | .. | .. |
| | 6/ 4/24 | 8,500 | 43 | 57 | .. | .. |
| | 3/ 5/25 | 8,000 | 52 | 48 | .. | .. |
| 3. | 12/31/24 | 17,000 | 70 | 30 | .. | .. |
| | 1/16/25 | 8,400 | 51 | 45 | 2 | 2 |
| | 1/26/25 | 7,700 | 37 | 60 | 3 | .. |
| | 10/23/25 | 7,550 | 41 | 56 | 3 | .. |
| 4. | 11/28/22 | 21,250 | 9 | 90 | 1 | .. |
| | 12/ 1/22 | 25,200 | 13 | 86 | 1 | .. |
| | 12/ 6/22 | 10,500 | 56 | 44 | .. | .. |
| | 12/ 8/22 | 8,250 | 41 | 59 | .. | .. |
| | 12/14/22 | 6,500 | 32 | 63 | 5 | .. |
| | 1/ 6/25 | 7,200 | 59 | 40 | 1 | .. |

SUMMARY—INFECTIOUS MONONUCLEOSIS

| | Cases | Counts | Total | W.B.C. | Poly. | Lymph. | Tran. | L.M. | Eos. |
|---|---|---|---|---|---|---|---|---|---|
| Table 1 | 9 | 15 | 185,750 | 12,385 | 38.4 | 56.5 | 2.4 | 2.6 | |
| 2 | 4 | 8 | 93,500 | 11,690 | 41.2 | 54.6 | 1.2 | 1.0 | 1.0 |
| 3 | 4 | 17 | 188,200 | 11,070 | 42.6 | 56.2 | .. | .. | 1.0 |
| | 17 | 40 | 467,450 | 11,685 | 40.7 | 55.8 | 1.2 | 1.2 | 0.7 |

The very close similarity in the total white and differential count by three independent groups of observers is striking. The character of the mononuclears is the outstanding factor in differential diagnosis and unfortunately this cannot be manifest in any tables such as these.

TABLE IV—BLOOD COUNTS IN HODGKIN'S DISEASE
(McAlpin, K. R. (19))

*Untreated Cases*

| Time Since Onset | Case | W.B.C. | Platelets | Neutro. | Lym. | Eos. | Tr. | Bas. | Myel. | Leuko-cytes |
|---|---|---|---|---|---|---|---|---|---|---|
| 3 Months | 1. | 13,000 | 680,000 | 89.6 | 4.6 | 3.0 | 2.2 | .. | .. | 0.6 |
| 3½ Years | 2. | 11,000 | 400,000 | 47.8 | 34.8 | 7.8 | 7.0 | 0.4 | 0.4 | 1.8 |
| 1½ Years | 3. | 10,900 | 36,000 | 86.2 | 9.4 | .. | 3.6 | 0.2 | .. | 0.6 |
| 3 Months | 4. | 10,000 | 150,000 | 78.4 | 18.3 | 0.3 | 3.0 | .. | .. | .. |
| 6 Weeks | 5. | 8,800 | 230,000 | 62.0 | 22.0 | 12.0 | 3.7 | 0.3 | .. | .. |
| 4 Years | 6. | 7,200 | 210,000 | 69.0 | 26.4 | 0.6 | 3.7 | 0.3 | .. | .. |
| 1 Year | 7. | 6,000 | 200,000 | 61.4 | 32.4 | 1.3 | 4.6 | 0.3 | .. | .. |
| 1½ Years | 8. | 4,900 | 150,000 | 67.4 | 26.0 | 2.6 | 3.2 | 0.8 | .. | .. |
| 8 Months | 9. | 4,200 | 150,000 | 54.4 | 31.3 | 5.0 | 3.0 | 6.3 | .. | .. |
| 2 Months | 10. | 4,000 | 180,000 | 71.6 | 20.6 | .. | 7.4 | .. | 0.2 | 0.2 |
| *Treated Cases* | | | | | | | | | | |
| 5½ Years | 1. | 10,000 | 340,000 | 79.6 | 3.0 | 0.2 | 17.0 | 0.2 | .. | .. |
| 5 Months | 2. | 8,200 | 350,000 | 71.8 | 17.6 | 2.4 | 7.6 | 0.6 | .. | .. |
| 2 Years | 3. | 7,000 | 370,000 | 76.4 | 13.4 | 4.8 | 5.0 | 0.2 | .. | 0.2 |
| 19 Months | 4. | 6,000 | 550,000 | 78.6 | 6.8 | 3.2 | 11.2 | 0.2 | .. | .. |
| 16 Months | 5. | 5,700 | 300,000 | 78.0 | 11.2 | 2.2 | 6.6 | .. | .. | 2.0 |
| 3 Months | 6. | 4,500 | 280,000 | 65.8 | 31.0 | .. | 2.8 | .. | .. | 0.4 |
| 15 Months | 7. | 4,300 | 470,000 | 70.8 | 20.0 | 3.8 | 3.6 | 1.2 | 0.6 | .. |
| 4 Months | 8. | 2,000 | 45,000 | 32.5 | 62.0 | .. | 5.0 | .. | .. | 0.5 |

TABLE V—BLOOD COUNTS IN HODGKIN'S DISEASE
(Cunningham, W. F. (53))

| Case | W.B.C. | Polys. | Lymphs. | L. Monos. | Tr. | Eos. | Baso. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|---|---|
| 1. | 74,000 | 91.7 | 3.3 | 2.3 | 2.4 | .. | 0.3 | 4,150,000 | 70 |
| 2. | 15,000 | 76.8 | 6.7 | 0.8 | 12.6 | 2.3 | 0.5 | 4,300,000 | 60 |
| 3. | 20,000 | 80. | 11.0 | 1.8 | 6.0 | 0.5 | 1.15 | 5.600,000 | 75 |
| 4. | 14,000 | 69. | 20. | 2.3 | 7.3 | 1. | 0.3 | 3,500,000 | 58 |
| 5. | 12,000 | 68. | 22.3 | 2.3 | 5.0 | 2.3 | .. | 4,360,000 | 68 |
| 6. | 11,000 | 78. | 11.5 | 3.3 | 5.8 | 0.6 | .. | 3,750,000 | 80 |
| 7. | 19,000 | 72.5 | 19.6 | 0.6 | 5.3 | 1.3 | .. | 5,550,000 | 90 |
| 8. | 16,000 | 73.5 | 17. | 0.5 | 7.0 | 0.6 | .. | 4,800,000 | 94 |
| 9. | 62,000 | 92.0 | 1.5 | 2.3 | 3.5 | 1.3 | 0.15 | 4,700,000 | 56 |
| 10. | 12,000 | 71.0 | 15. | 5.3 | 6.3 | 1.5 | 0.6 | 4,000,000 | 68 |

TABLE VI—BLOOD COUNTS IN HODGKIN'S DISEASE
(Lemon, W. B. and Doyle, J. B. (52))

| Case No. | W.B.C. | Polys. | Lymphs. | Large Monos. | Eos. | Baso. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|---|
| 1. | 23,900 | 48.0 | 23.3 | 4.3 | 27.7 | 0.7 | 4,400,000 | 80% |
| 2. | 12,800 | 81.7 | 9.3 | 2.7 | 1.0 | 0.3 | 3,770,000 | 50 |
| 3. | 5,200 | .. | .. | .. | .. | .. | ..... | 65 |
| 4. | 5,200 | .. | .. | .. | .. | .. | 4,720,000 | 85 |
| 5. | 3,000 | 59.7 | 30.7 | 9.0 | 0.0 | 0.7 | 3,250,000 | 57 |
| 6. | 7,000 | 86.7 | 5.7 | 6.7 | 0.7 | 0.3 | 3,720,000 | 61 |
| 7. | 13,200 | 78.7 | 12.7 | 5.0 | 3.7 | 0.0 | 4,880,000 | 88 |
| 8. | 8,600 | 81.0 | 10.0 | 6.3 | 2.0 | 0.7 | 5,240,000 | 70 |
| 9. | 8,200 | 50.0 | 36.3 | 10.0 | 2.7 | 1.0 | 4,040,000 | 68 |
| 10. | 23,000 | 85.0 | 8.7 | 3.0 | 3.3 | 0.0 | 4,510,000 | 64 |
| 11. | 10,000 | 65.7 | 18.0 | 15.3 | 0.0 | 1.0 | 4,060,000 | 64 |
| 12. | 12,200 | 85.0 | 6.7 | 6.3 | 2.0 | 0.0 | 4,400,000 | 70 |
| 13. | 8,600 | 86.3 | 5.0 | 4.7 | 3.3 | 0.7 | 3,760,000 | 55 |
| 14. | 16,400 | 89.0 | 6.5 | 4.5 | 0.0 | 0.0 | 3,260,000 | 47 |
| 15. | 19,500 | 83.5 | 9.5 | 5.5 | 1.5 | 0.0 | 4,880,000 | 70 |
| 16. | 13,800 | 82.0 | 12.0 | 4.0 | 2.0 | 0.0 | 4,720,000 | 74 |
| 17. | 7,800 | .. | .. | .. | .. | .. | 3,760,000 | 55 |
| 18. | 8,400 | .. | .. | .. | .. | .. | 4,400,000 | 58 |
| 19. | 4,900 | 90.0 | 5.0 | 5.0 | 0.0 | 0.0 | 4,400,000 | 53 |
| 20. | 8,600 | .. | .. | .. | .. | .. | 3,460,000 | 45 |
| 21. | 17,400 | 84.0 | 11.5 | 3.5 | 1.0 | 0.0 | 4,260,000 | 68 |
| 22. | 10,200 | 76.0 | 19.5 | 3.5 | 1.0 | 0.0 | 4,800,000 | 62 |
| 23. | 15,400 | 87.5 | 7.5 | 5.0 | 0.5 | 0.0 | 4,240,000 | 50 |
| Average | 13,370 | 77.7 | 13.2 | 6.1 | 2.9 for 18 cases | 0.3 | 4,230,000 | 67 |
| | | | | | 1.5 for 17 cases | | | |

TABLE VII—BLOOD COUNTS IN HODGKIN'S DISEASE
(Symmers, D. (54))

| Case No. | W.B.C. | Polys. | Lymphs. | Large Monos. | Tr. | Eos. | R.B.C. | HB. |
|---|---|---|---|---|---|---|---|---|
| 1. | 7,000 | 76 | 20. | 2. | 2. | .. | 2,300,000 | 35% |
| 2. | 18,000 | 94.5 | 2.5 | 1.5 | 1.5 | .. | ..... | .. |
| 3. | 2,200 | 85. | 10 | 2 | 3 | .. | 3,800,000 | .. |
| 4. | 13,200 | 92 | 5 | 2 | 1 | .. | ..... | .. |
| 5. | 6,700 | 69 | 24 | .. | .. | 7 | 2,568,000 | 60 |
| 6. | ..... | .. | .. | .. | .. | .. | ..... | .. |
| 7. | 5,200 | 64 | 21 | 6 | 9 | .. | 2,910,000 | .. |
| 8. | 14,800 | 59 | 39 | .. | 2 | .. | 2,400,000 | 18 |
| 9. | ..... | .. | .. | .. | .. | .. | ..... | .. |
| 10. | 16,200 | 92 | 7 | .. | .. | 1 | 3,800,000 | 70 |
| 11. | 17,500 | 80 | 9 | 3 | 2 | .. | 4,200,000 | 65 |
| 12. | ..... | 78 | 17 | (5 mast cells) | | .. | 4,400,000 | .. |
| 13. | 6,600 | 66 | 20 | 10 | 4 | .. | 4,912,000 | .. |
| 14. | 11,000 | 80 | .. | .. | .. | .. | 2,400,000 | .. |

SUMMARY OF HODGKIN'S DISEASE

| | Cases | Counts | W.B.C. | Poly. | Lymph. | Eos. | Tr. | Bas. | Mye. | Platelets |
|---|---|---|---|---|---|---|---|---|---|---|
| Table 7 | 14 | 11 | 10,765 | 80.9 | 14.6 | 0.7 | 2.0 | .. | 2.2 | ..... |
| Table 4 | | | | | | | | | | |
| Untreated | 10 | 10 | 8,000 | 68.8 | 22.6 | 3.3 | 4.1 | 0.3 | .. | 238,600 |
| Treated | 8 | 8 | 5,960 | 69.2 | 20.6 | 2.1 | 7.3 | 0.3 | .. | 338,125 |
| Table 5 | 10 | 10 | 25,500 | 77.2 | 12.8 | 1.1 | 6.1 | 0.3 | 2.2 | ..... |
| Table 6 | 23 | 23 | 13,370 | 77.7 | 13.2 | 1.5 | .. | 0.3 | 6.1 | ..... |
| Average | 65 | 63 | 12,720 | 74.8 | 16.8 | 1.7 | 3.9 | 0.24 | 2.1 | |

This summary is self explanatory. Relatively wide variation in the total white count is noted and though the differential count tends to greater similarity, there is nothing characteristic.

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# Roentgenography in its Relationship to Clinical Findings in Pulmonary Tuberculosis*

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A GREAT deal of confusion exists in the interpretation of roentgenological chest findings in terms of symptoms, clinical findings, pathological findings, and prognosis. Many of our roentgenologists are laboriously trying to master details of what are supposed to be pictures characteristic of certain types of pulmonary tuberculosis, without considering any basic reason for the production of these types. The variations are so numerous and changing that one would be kept constantly on the jump to keep a patient correctly tabulated. No one can be surprised at the controversies that are continually arising between clinician and roentgenologist. Certain broad principles will greatly harmonize the clinical and roentgenological findings. These principles today seem to offer the easiest explanation of events, and although future thought may evolve something better, we have at least a working hypothesis for the present. The more of the clinical and pathologicla side the roentgenologist knows, the better fitted he eventually becomes to interpret the roentgenographic plate. No one field of diagnosis is complete in itself although there is a high proportion of cases where clinical methods alone suffice to establish a positive diagnosis, and again another high percentage of cases where the roentgenograph interpreted by a competent roentgenologist supplies evidence sufficient for a definite diagnosis. Then again we have a large group of atypical cases where the roentgenologist should be sufficiently skilled to combine clinical information and other features of the case with his roentgenological findings to arrive at the proper interpretation. When clinical and roentgenological findings all favor the same diagnosis we feel justified in making positive statements. There must be a limit to one's indecision, and contrary to the opinion of many, the roentgenologist should avail himself of all clinical data.

My object here is to discuss briefly the value and limitations of the several methods of examination, and explain the reasons for some of our roentgenographic and clinical manifestations. A number of factors enter into the consideration of the tuberculosis lung reaction, and only brief references can be made without making this paper too voluminous. It has been shown experimentally (1) that the

first response to the tuberculosis bacillus invasion is the same as the response to any foreign body, and that in a few weeks the reaction takes on the reaction characteristics of tuberculosis. Tuberculous reinfections appearing subsequently to this are all modified in their character because of the previous infection. The initial and subsequent reinfections (unless overwhelming) produce a hypersensitiveness to tuberculo-protein which varies with each individual and with the age and extent of the lesions. This hypersensitiveness manifests itself by an exudation reaction about old and new areas of tuberculous involvement, when tuberculous reinfection takes place. The skin tuberculin tests usually show a marked reaction when hypersensitiveness or allergy is high, although experimental work recently done would indicate that the true allergic state may not manifest itself by the reaction to skin tests, and in these cases has been termed "latent allergy".(2) The focal reaction, however, is supposedly of fairly constant behavior under similar conditions. The body foci respond to reinfection exudatively or productively (fibrosis); like any inflammatory process the object of the reaction is supposedly protective in great measure. The infection is first corralled. If fibrosis predominates, shrinking avascular scar results. Without vascularity toxic symptoms must necessarily diminish. If there has been more of an exudative reaction, this exudate will gradually absorb in great part, caseocalcareous material may form, or we may have a tuberculous abscess with cavity resulting. In younger people the lymphatic system is generally more "open", as they have not been subject to so many lung infections, and the tuberculous infection may be kept in the lymphatic system (lymph follicles and nodes) which condition is usually well-borne by the individual in childhood, although primary tuberculosis of adult life is often very serious. Tuberculosis of the lungs involves the lymphatics or lymphoid tissue primarily and then spreads to the contiguous lung tissue. Phagocytosis is the means of removing bacilli into the lymphatic system from the surrounding lung tissue, blood channels, and air passages.

Allergy which determines in great part the tissue reaction or pathological activity is not the sole guide to immunity. It is well known that the various organs of the body may detroy tubercle bacilli without the production of any great local reaction. The "innate" immunity (3) of each individual varies markedly and is perhaps often the chief determining factor in the final outcome of the tubercle bacillus invasion. It is difficult to reconcile ourselves to opinions which ignore or belittle the idea of variations in "innate" immunity. Prognosis depends upon numerous factors which we cannot discuss here. It must be recognized that the exudative and productive reactions are what we attempt to determine both by roentgenograph and by physical examination. This however does not determine the whole story of a case. The future course of any tuberculous lesion cannot always be guaged by the existing pathological activity. A reaction benefitting

one case may be the cause of a fatal outcome in another, but we can always be sure that exudate means that the body is reacting to an irritant. This reaction may be stimulated locally or may be precipitated by more distant stimulants. These stimulants may be specific (tuberculous reinfection or tuberculin) or they may be non-specific. (4) The non-specific stimulants or irritants may be organic or mineral substances, fatigue toxins, starvation, trauma, or may be non-specific bacterial infections, such as abscessed teeth, infected tonsils, etc. The reactivation by quiescent lesions can conveniently be explained on the theory of "balanced allergy" advanced by Victor Vaughan; (5) the specific predisposing cause of allergy being the tuberculo-protein of the tuberculous infection and the exciting cause being specific or non-specific; the tuberculous allergy in such cases by itself not being sufficient to precipitate a marked inflammatory reaction, but is capable of doing so under the influence of an added specific or non-specific irritant. Complete avascularization of the area would prevent demonstrable reactivation, and removal of either the exciting cause or the predisposing cause, as in other allergic diseases, would eliminate the reaction.

A healing lesion is accompanied by an increasing allergy and with this our immunity becomes increasingly greater. Like other infections complete cure is attended by a gradually diminishing immunity. A healed lesion of long standing may be accompanied by very little immunity, and the patient may again under conditions of lowered vitality be liable to a reinfection. We all see repeated cases exhibiting widespread markedly exudative areas. It would seem logical to assume that these areas often represent a later stage in the reinfection. It is probable that the initial number of bacteria reaching the new lung areas of infection may be quite few, and unhindered by body resistance, develop rapidly and may be respread in various ways, amongst which may be through inhalation and through the phagocytic mobile large monocyte or endothelial leucocyte. By this time allergy, soon developed, comes into play to produce our exudative reaction. Animal experimentation showing the necessity of massive inoculation to produce secondary and tertiary reinfection does not consider the allergy of the animal at the time of inoculation, which is probably high. We know that in humans, with high allergy, aspiration of a large amount of infected sputum into a bronchus will produce a reinfection with a most violent reaction (lobar pneumonia), but we hardly expect minute infections to gain much headway. Our initial allergy upon reinfection it seems would naturally determine in great part the extent of the involvement and subsequent inflammatory reaction. It would seem, therefore, that one must consider both endogenous and exogenous sources of infection.

After the above brief summary of the tuberculous reaction which we find is dependent upon the hypersensitiveness of the individual and the vascularity of the infected area we may more readily inspect our methods of

investigating these local reactions. It is generally felt that chest findings can best be interpreted in terms of pathological activity or in other words "tissue reaction". We attempt to determine the degree and extent of this reaction. This reaction while important may be entirely lacking in many cases which may soon prove serious. We are often encountering cases where our first intimation of pulmonary tuberculosis is hemorrhage. We try to rule out all other possibilities (infarcts, mitral stenosis, malignancies, trauma, varices, parasites, etc.) and concentrate on finding an active tuberculous lung lesion. Maybe we obtain evidence of an old scar or retracted apex but we often cannot determine activity. A roentgenographic plate shows nothing and yet we feel certain it is due to active tuberculosis. With massive coagulation necrosis accompanying a markedly exudative reaction and cavity formation, hemorrhage or blood oozing may occur as we should expect, but this process is different. There is diminished allergy and with this a lack of immunity, and a very small tuberculous process involves a blood vessel with accompanying hemorrhage. It is probable that such erosion of very small blood vessels which should normally be most resistant tissue occurs as proof of lowered vitality and lack of immunity, and the patient must be considered as potentially serious, regardless of symptoms and other findings. One must not lose sight of the fact, however, that it may not require much of an altered lung condition to produce a pulmonary hemorrhage. The slight pulmonary congestion in early mitral stenosis, for instance, is quite sufficient to produce hemorrhage. Miliary tuberculosis cases, in which we have great numbers of tubercles, rarely live long enough or are able to respond to the infection with enough developed allergy to produce a noticeable exudate as seen in the roentgenograph or microscopic section. With smaller showers of tubercle bacilli the process may limit itself to the region of the lymph follicles in the form of a peribronchiolitis, the infection not being overwhelming soon produces sufficient allergy to permanently prevent spread of the infection and soon leads to cure. It is the allergic response which determines in great mesure the future course of the infection. Activity which we are unable to demonstrate clinically or roentgenographically does not, as we have just seen, justify us in completely ignoring the general condition of the patient, or treating the case as being in no wise worthy of special attention. Another somewhat similar condition is dry pleurisy. We may or may not elicit a friction rub and the roentgenograph may show nothing unusual, yet many of these pleurisies are the forerunners of more active tuberculosis.

In considering lung lesions which present evidence of an inflammatory process or "activity" we find a great deal of variation in the degree of so-called "activity". Our lesions may be so active as to produce symptoms and physical and roentgenographic findings which are difficult to differentiate from other acute non-tuberculous lung infections. Sputum examination, when positive for tubercle bacilli, is often the only possible reliable clinical aid in

diagnosis, and roentgenographically one must wait until the lesions have had sufficient time to produce the usual characteristics of tuberculosis. A consideration to be kept constantly in mind is the individual "reaction factor" toward disease. No two people react alike to the same kind or degree of tuberculous infection, or any other kind of infection. We often see people actively at work, oblivious of anything wrong, come in for chest examination because of the knowledge that a "cold should not hang on so long", to find an advanced tuberculous condition present. Then again the patient may show marked symptoms with very few roentgenographic or physical findings. So many factors are concerned in the production of symptoms and findings that each case becomes individual in its behaviour. Clinical activity may bear no relationship to the severity of the pathological process. A quotation from an article by Medlar and Kastlin (6) perhaps puts this more comprehensively: "It is acknowledged that pathological activity does not mean a clinical or manifest disease in tuberculosis; but the common occurrence of a clinical breakdown after a clinical arrest of the disease would lead us to believe that pathological activity had not subsided with the abatement of clinical symptoms". The subjective feelings of the patient and the abatement of clinical symptoms are no doubt important in prognosis. In pneumonia our crisis which leaves our patient feeling better and on the highroad to recovery is accompanied by very little actual immediate alteration in the pathological lung condition. Tuberculosis, however, is a slow-moving infection and recovery is gradual. The physician in his physical examination is attempting to determine pathological activity. Positive physical findings are important, but an absence of evidence of an active process may be most misleading. A subnormal temperature is common in many non-tuberculous individuals, an elevated temperature may be entirely lacking, an increased pulse rate is perhaps a better guide to activity but may accompany numerous other confusing conditions. Loss of weight, nightsweats, cough, fatigue, restlessness and irritability generally accompany outspoken cases, but an earlier diagnosis is most important. On physical examination, flattening of the chest wall, retracted interspaces, deficient expansion, lagging, etc., are all aids. Most of these physical findings may occur with emaciation from any cause. On palpation Pottenger's sign is too uncertain, vocal fremitus is of slight value, and our percussion note of no value in determining slight degrees of exudate as distinguished from healed fibrotic areas. The low spinal dullness and D'Espine sign, the only evidence one hopes to obtain in pure hilum node tuberculosis, is notably untrustworthy. With regard to auscultatory findings, these rarely add anything of importance. Râles, the subcrepitant variety properly interpreted, may be absent from even markedly exudative areas and when found may persist long after the pathological process has completely healed. It is for these reasons that we have been afflicted with our innumerable never-ending attempts to establish evidence of tuberculous activ-

ity by clinical and laboratory tests; the various tuberculin tests, the numerous clinical tests more recently advocated, the differential blood counts with relation to the predominance of large monocytes, lymphocytes, and Arneth counts, the temperature and pulse reactions after exercise, etc. The "Sedimentation" test is finding too many exceptions to offer information that cannot be more certainly diagnosed by other means.

In discussing the roentgenographic findings I shall not describe the detailed anatomy of the lungs and minute accounts of the more recent theories and fine points differentiating tuberculosis from other diseases. I will just repeat that tuberculosis of the lungs occurs primarily in the lymphoid tissue of the lungs and may by extension invade the contiguous lung tissue. The exudate accompanying the inflammatory process is what determines the activity of a lesion on the roentgenographic plate. When the exudate completely fills one or more secondary lung lobules we have the so-called Dunham's triangle or fan. Different cases present different degrees of exudate about the foci of tuberculous infection. This exudate is determined by the inflammatory reaction which in turn depends in great part upon the patient's hypersensitiveness and the vascularity of the area. Fibrotic and other changes will affect this vascularity, which may go to complete avascularization and cure. The amount of toxic absorption taking place from completely fibrosed areas may be sufficient to give toxic symptoms when these areas are very large. Restimulation of a previously infected area may be due to various agents described above. As the inflammation or activity subsides the exudate subsides. This is brought about in several ways, the avascularization of the area through fibrotic and calcific changes in the infected areas, and through digestion, reabsorption and neutralization of the focal products. The presence of exudate means that irritative products are still present and that avascularization through fibrosis is at least not complete. The beading and furring of markings speak for small amounts of exudate, while the large undemarcated clouded areas represent the more marked exudates. The former tax one's knowledge of tuberculous infection. The various modifications and increase of lung markings accompanying different lung lesions are in a certain number of cases indistinguishable, but a very high percentage of these milder lung lesions are typical and can be diagnosed with certainty, qualitatively and quantitatively. A subsequent roentgenographic re-examination will clear up many of the previously doubtful ones.

The roentgenogram merely determines the degree and extent of exudate, which is just as true a measure of tuberculous activity as the reaction about any other kind of infection is a measure of the inflammatory process, or in other words it determines active pathology which may or may not have a corresponding clinical picture, which must necessarily be conjointly considered. Properly taken roentgenograms will rarely miss showing lesions which can be definitely shown clinically. Infraclavicular infiltrations which have

recently been so copiously described are difficult to find in any way other than roentgenographically. The presence of large calcific and fibroid areas in the lungs give undoubted evidence of previous tuberculous lung infection, although we frequently can elicit no history of anything suggesting such an infection. Tuberculous lesions do heal, even without medical advice, so that the mild forms can very often be diagnosed negative without doing any great harm to the patient. How many cases with slight afternoon rise of temperature and other indefinite symptoms can be positively diagnosed tuberculosis clinically? Tuberculosis is often diagnosed in these cases by a process of eliminating other diseases, basing the entire diagnosis on the fact that tuberculosis is so common. Gross autopsies will never be of service in helping to differentiate these very slight degrees of activity, and it would be too laborious to check up these cases with large numbers of serial microscopic sections so as to catch the proper areas. The presence of tubercle bacilli in the sputum rarely occurs in anything but lung lesions with gross roentgenographic evidence, and when found give no hint of their source. Even a gross lung lesion may frequently be continuously bacteriologically negative. It is true that exudate in a roentgenographic plate may be so slight as to represent activity of only academic interest, but it is always more satisfactory to make the diagnosis as fine as possible hoping that the physician in charge of the case will grasp the exact meaning of such degrees of activity. It seems almost possible at the present time to differentiate cases of mere reactivation, as determined by furring of old markings, from cases showing new areas of tuberculous involvement. The former may possibly be in great part responsible for many of our numerous easily controlled cases, as our superimposed irritant may be of an entirely non-specific and temporary nature. With regard to hilum tuberculosis of childhood there are numerous confusing conditions which produce hilum nodal swelling and unless we find undoubted evidence of tuberculosis in the lung parenchyma or other evidence of tuberculosis, such as tuberculous adenitis and calcified nodes, we cannot be certain of the condition. Poorly exposed films will often not differentiate between hilum calcifications and bronchial cross-sections. That all hilum node calcification must be tuberculous is still not definitely proven. We know calcific deposits in other locations may be of non-tuberculous origin (lime deposits in sheath of supraspinatus tendon, "subdeltoid bursitis", calcification of tumors, etc.)

## Summary

Much confusion exists in the interpretation of roentgenographic lung findings. Much of this confusion can be cleared up by learning the fundamental principles which are responsible for these findings rather than by trying to master pictures supposedly characteristic of different types of tuberculosis. We attempt roentgenographically and by clinical means to determine the same thing, namely, the "activity" of a lesion. Exudate about a lesion signifies activity, and this exu-

date depends in great measure upon the developed allergy. The individual "reaction factor" to disease is a most important consideration. As the activity or exudate subsides we find corresponding evidence in our roentgenograph, which presents the actual pathological process to us. This evidence often cannot be obtained by other means. Numerous other factors must. however, be also considered in prognosis.

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# Medical Management of Gastric Ulcer*†

By G. G. Richards, *Salt Lake City, Utah*

THE most important single factor in the treatment of a gastric ulcer is an accurate diagnosis. To subject a patient to a long period of careful dieting and control of his acid for an ulcer that does not exist is wasted effort and certainly not appreciated by the patient. To operate on him and perform a needless gastroenterostomy is not to be excused. To attempt an ulcer cure medically for a malignancy of the stomach, whose only hope lies in surgery, will remain a face in the darkness of one's own conscience even after his mistake is hidden in the grave. Great responsibility, therefore, rests upon the clinician and the roentgenologist who first make a diagnosis of an intragastric lesion, and secondly differentiate a benign from a malignant ulcer.

For many years we, at the Salt Lake Clinic, have been ardent admirers of the Mayo Clinic. Naturally, we became their disciples in the fear of the relationship between gastric ulcer and cancer. Consequently, we have, in the past, almost always recommended that gastric ulcers be treated surgically.

Our complications, however, from partial gastrectomies or other operative procedures, sufficiently radical to completely remove the ulcer, were frequent enough to make us feel that the dangers attendant upon such operations might be greater than the probability of the ulcer being or becoming malignant in carefully selected cases.

Acting upon this thought, the medical department of our Clinic became courageous about two years ago and decided to treat medically all cases of ulcer of the stomach in whom we could not find any definite evidence of the lesion being malignant. We argued that a three weeks delay before resorting to surgery would not be very serious and that medical and dietetic management during this period would probably improve the condition of the patient even as a preoperative measure, and that we could use this as a sort of therapeutic test. We assumed that a benign ulcer would show definite signs of improvement clinically and from an X-ray standpoint, while an ulcer that was already malignant would refuse to respond so favorably.

Our courage was also supported by the fact that some of our most authoritative pathologists have expressed themselves, that there is very little danger of a benign gastric ulcer becoming malignant, and that Dr. McCarty of the Mayo Clinic may be mis-

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†Read before the Southwest Idaho Medical Society on May 9, 1928.

taken in the interpretation of his so-called cancer cell.

The only dangers attached to such medical treatment, we felt, were

First, that of the ulcer becoming malignant.

Second, that of perforation or hemorrhage which occurs less frequently during proper management.

During the last two years we have had twenty-four cases of gastric ulcer under observation. Of this number, ten were operated because of a history of massive hemorrhage, or perforation, or because the X-ray examination was quite suspicious of a carcinomatous ulcer.

Of the remaining fourteen patients, eleven were treated medically, seven in the hospital and four as ambulatory cases. Three cases refused treatment and were lost track of.

The medical management was preceded by removing all focal infections.

When possible, they were kept in bed most of the first two weeks. If in much pain associated with tenderness, heat was applied to the abdomen. In those cases with marked pylorospasm and retention, belladonna was used.

The free acid of the stomach was fairly well controlled in most of the cases by the use of the alkalies, soda bicarbonate, calcium carbonate and magnesium oxide. We have followed the suggestion of Crohn and others, using small doses, five to ten grains, one or two times between the feedings. We are thoroughly convinced that this method of using from 60 to 120 grains of alkalies, in the twenty-four hours, has distinct advantages over the large doses formerly prescribed by Dr. Sippy, principally in that the small frequent doses do not cause alkalosis or a reaction rise in the production of HCl in the stomach as occurs after the ingestion of large doses.

Determinations as to the control of free acid were made by stomach aspirations at various times in the twenty-four hours.

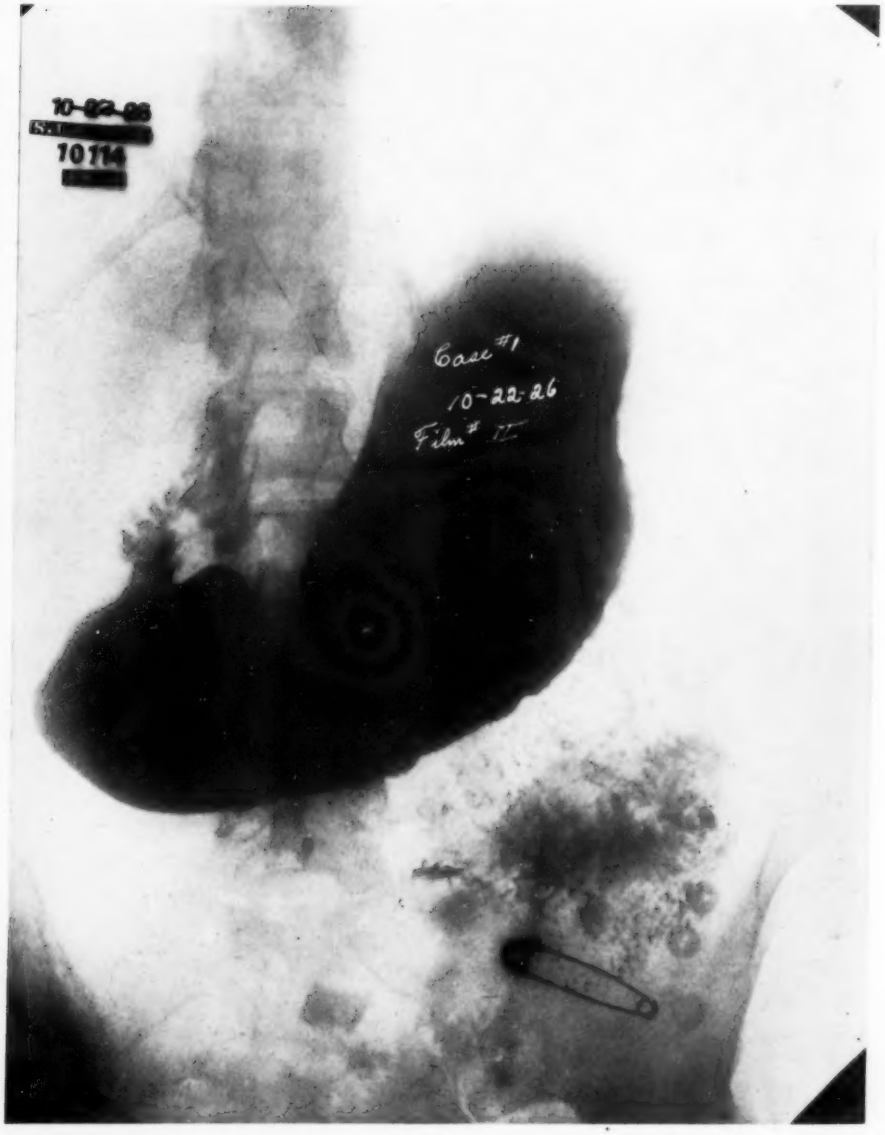
We feel that the pyloric sphincter is probably the most important factor in the production and control of hyperacidity, because it determines the emptying time and regulates the regurgitation of the alkaline duodenal contents into the stomach.

The nervous system is certainly largely responsible for the pyloric action. This is often demonstrated by the difficulty experienced in controlling the gastric acidity and the ulcer syndrome in patients burdened by worry, fatigue or nervous excitement. Relief of these conditions is very important. Sedatives may be necessary at the beginning.

The diet which we have used is a modified Sippy type. It has been our experience that a careful diet is necessary for six months to a year and that it is never safe for an ulcer patient to become careless with his diet. In order to insure the cooperation of the patient, he must first be educated to the reasons and necessity for this prolonged dieting. Second, the diet must be sufficiently nourishing, simple and convenient to enable him to make a living and enjoy life while on it.

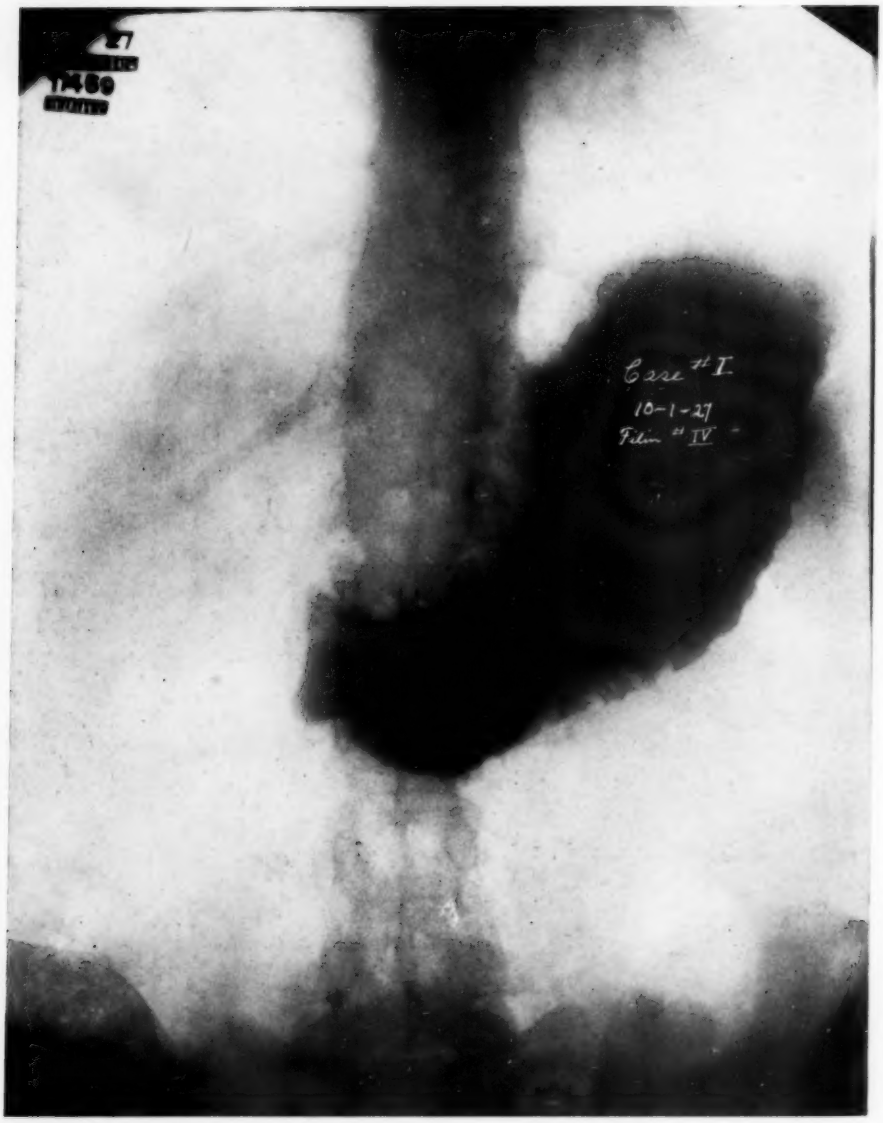
The continuance of the frequent milk feedings is probably the most important single factor in the diet of these patients.

CASE 1. FIGURE 1. Showing the ulcer before treatment.




CASE 1. FIGURE 2. Showing the crater entirely gone seven weeks after beginning of treatment.

CASE 1. FIGURE 3. Shows no sign of a return of the crater three months after treatment.




CASE 1. FIGURE 4. Shows a perfectly normal stomach thirteen months after beginning treatment, during which time this patient has gone through a normal pregnancy.

CASE 2. FIGURE 1. Shows a very large crater at the beginning of treatment.

CASE 2. FIGURE 2. Showing the crater almost entirely disappeared 28 days after beginning of treatment.

CASE 2. FIGURE 3. Shows the crater entirely healed two and one-half months after begnining treatment.

CASE 3. FIGURE 1. Shows a large crater with a very broad base at the beginning of treatment.

We have attempted to re-examine all the cases about every two weeks during what might be called the probation stage of this medical management.

### Treatment of Complications

*Hemorrhage*

Mild bleeding is very common in gastric ulcers. It does not require special treatment unless it persists after a week of diet and medical management.

Acute profuse hemorrhage calls for immediate and very definite measures. Lowering of the blood pressure suddenly often is very effective in helping the physiological processes to stop the bleeding. Instead of placing the patient in a reclining posture, support him in the upright position until he faints, then slowly put him to bed and keep him as quiet as possible. A blood pressure apparatus may be applied to each extremity to reduce the amount of blood in the abdomen. A hypo of morphine is very necessary as a sedative to the nervous system and particularly to the peristalsis. It should be repeated every six to eight hours as necessary during the first twenty-four hours.

An ice bag over the epigastrium may have some specific beneficial effect or it may help merely by making it necessary for the patient to remain quiet in order to keep the bag on his abdomen.

If nausea and vomiting persist, stomach lavage done very carefully is advisable. A small catheter stomach tube can be inserted just within the cardia and not cause gagging or any traumatism to the ulcer. Sometimes a solution of 1:1,000 ferric chloride seems to have a definite beneficial effect. Some advise leaving one dram of 1:1,000 adrenalin chloride in the stomach after the lavage, but I am always afraid of the reaction rise in blood pressure after adrenalin.

The volume of blood must be restored to the patient. Just how this should be done will depend upon the severity of the hemorrhage. As a rule, normal saline and glucose by bowel or occasionally by vein are sufficient. Some cases require immediate transfusions because of the amount of the loss. Smaller quantities of blood, 300 c.c., repeated if necessary are safer than large amounts.

Patients who have had a tendency to repeated small hemorrhage are greatly benefited by transfusions. Some cases, with anemia following a hemorrhage, do not recover well upon the usual medical management. A transfusion will often act as a splendid tonic and start them on a more rapid road to recovery.

We have never found any coagulant as efficient in promoting clotting as the injection of whole blood either into the vein or subcutaneously. Occasionally calcium intravenously has seemed to be of benefit.

*Feeding a case after a hemorrhage*

Everything by mouth is withheld for twenty-four hours. Water in one ounce doses is then begun every one-half hour, increasing to two ounces on the second day. Milk ℥II and lime water ʒII every two hours is given on the third day and is increased each day

CASE 3. FIGURE 2. Shows the crater only about half its original size five weeks after beginning treatment.

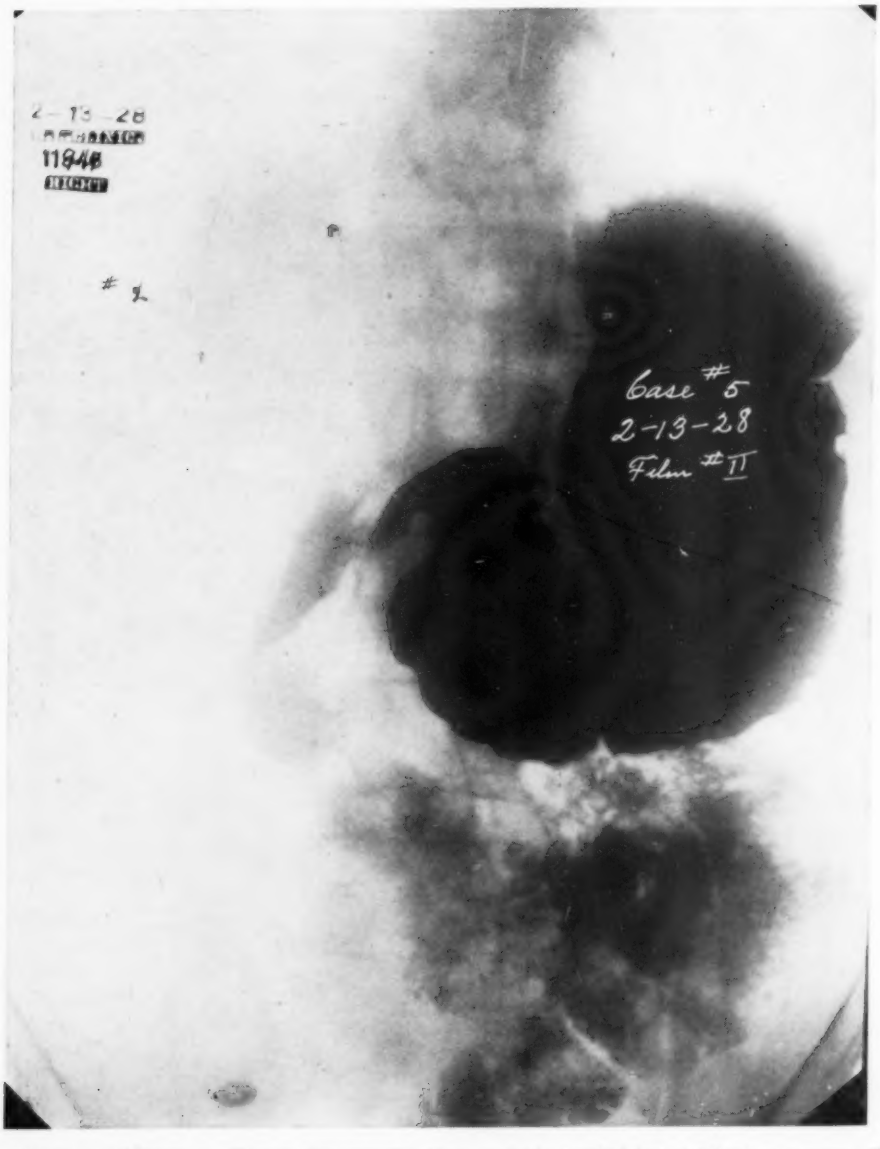
Case 3. Figure 3. Shows the crater almost entirely gone nine weeks after beginning treatment.

CASE 3. FIGURE 4. Shows no sign of a crater nine months after beginning treatment.

CASE 4. FIGURE 1. Shows a huge crater at the beginning of treatment.

CASE 4. FIGURE 2. Shows this crater entirely gone nine months after treatment. No improvement in the first month when he had a severe gastric hemorrhage, after which his badly infected teeth were removed and he made rapid progress.

CASE 5. FIGURE 1. This patient had a perforated pyloric ulcer six years ago, resulting in the above deformity. The gastric ulcer is apparently of recent origin.




CASE 5. FIGURE 2. Shows the gastric ulcer entirely healed but medical treatment did not influence the obstruction and deformity at the pylorus.

until the usual medical diet for ulcer is attained.

Operation during or immediately following a profuse hemorrhage is certainly to be avoided, except in cases where all possible medical help has failed and the condition is alarming.

*Gastric Ulcer with pyloric obstruction*

The treatment of this condition depends upon the degree and character of obstruction and upon the presence or absence of toxemia. Mild obstruction will usually yield to the medical management and belladonna. If the obstruction does not so respond, the case should be referred to surgery. These cases usually have definite symptoms and changes in blood chemistry indicative of a toxemia. This is especially true if they have been taking large amounts of alkalies. Their symptoms vary from loss of appetite, headache, drowsiness and nausea to extreme restlessness, muscular irritability or even tetany. The urine becomes scanty and contains large amounts of albumin and casts and it can easily be mistaken for a nephritic urine.

Blood chemistry reveals an alkalosis with a $CO^2$ combining power sometimes up to and above 100—a high urea and a low chloride.

Recognition of this condition should be made early and immediate treatment begun. It consists in stopping the alkalies immediately, which, by the way, should be given with very great care, if at all, in cases of definite pyloric obstruction. Infusions or enteroclysis, or both, of a five or ten per cent glucose and one percent salt should be given immediately and daily in amounts totalling 2500 c.c. to 3000 c.c. The infusions of glucose must be given very slowly or a large part of it will be lost through the kidneys. Insulin can also be given to aid in the utilization of the glucose.

The stomach should be carefully emptied each morning and evening.

The diet should be of such nature as will remain liquid while in the stomach as soups, gruels, orange juice, Jell-O, custards, etc.

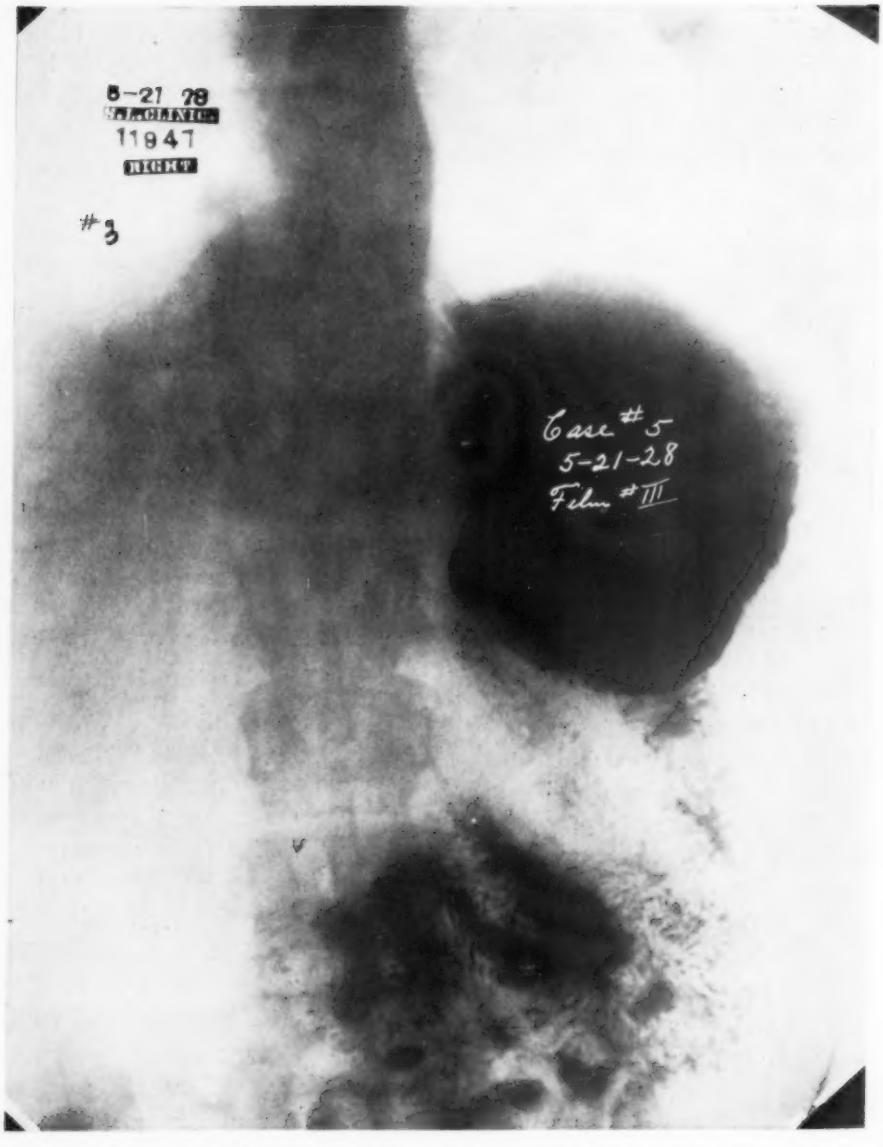
*Perforation as a complication*

Many gastric ulcers show a tendency to perforate. If the perforation is acute and complete, immediate operation is imperative. If it is incomplete and chronic, as many are, the same medical management as before outlined may be tried.

The summary of the results of treatment in this group is as follows:

Only two subsequently came to operation, one a foreigner who failed to remain on a diet after leaving the hospital. The other was a very neurotic maiden lady of fifty-four years whose many idiosyncrasies toward foods made a proper diet impossible. Two of the group died, but neither from their ulcer. One case, a man (E.P.) a miner, aged sixty-eight, died from a severe pulmonary fibrosis and a degenerated myocardium. The other, a man (E.O.) age sixty-two, died with uremia from a bad nephritis and a decompensated endocarditis.

Our results have been based upon the subsequent clinical history and X-ray findings.




CASE 5. FIGURE 3. Shows the stomach after a partial gastrectomy with no sign of return of the gastric ulcer.

CASE 6. FIGURE 1. Shows a small crater at the beginning of treatment.

CASE 6. FIGURE 2. Shows no signs of the crater four and one-half months after treatment.

CASE 7. FIGURE 1. Shows a very deep crater at the beginning of treatment.

CASE 7. FIGURE 2. Shows only partial healing of the ulcer. This patient was not seen between the dates of these two X-ray films and remained on a careful diet but a short time. He did, however, take alkalies during this period.

We failed to get temporary improvement in only one case, the maiden lady above mentioned.

We have had mild relapses in four cases, which could be attributed to dietetic indiscretions or mental worries.

We have not regretted any attempt which we have so far made. We have not included in this list any of the cases in the last six months, so we feel reasonably safe that none of these ulcers were malignant. We hope that future developments will not make us feel that we have been fool hardy in this medical treatment of some ulcers of the stomach when such an institution as the Mayo Clinic recommend surgery in all cases of gastric ulcer.

## Conclusions

1. This experience has convinced us that in some properly selected cases of ulcer of the stomach, medical treatment is justifiable.

2. These cases should be under close observation and have rechecks at frequent intervals.

3. Benign gastric ulcers, in our experience, respond more readily to medical management than duodenal ulcers and are less apt to have resultant deformities.

4. So far, we have seen no evidence of malignant degeneration in any case.

The accompanying X-ray films are self-explanatory. They belong to a part of the group in whom the X-ray pictures best illustrated the lesion. The remaining cases, not here illustrated, showed equally satisfactory results.

# Experimental Study of Acquired Resistance of the Rabbit's Renal Epithelium to Mercuric Chloride*†

By Warren C. Hunter, M.A., M.D., *Portland, Oregon*

In a previous paper I (1) have shown that a high degree of resistance to the injurious effects of uranium in the kidney can be experimentally produced. In a considerable number of rabbits it was found that 54 to 96 times the quantity of poison known to kill original renal tubular cells was insufficient to damage the regenerated epithelium in the same location. After administration of even the largest doses of uranium the metal was still excreted by the kidney and this together with the lack of histologic evidence of cell injury was considered to be proof of an acquired resistance on the part of the new epithelium. In the previous study the literature on experimental chronic nephritis and that portion of the experimental work of Gil y Gil (2) concerned with acquired immunity of the kidney for uranium nitrate has been reviewed in detail and need not be repeated here. It is sufficient to state that, as with uranium nitrate, Gil y Gil is the only previous investigator who has attempted to induce in the kidney an immunity for mercuric chloride. On this account it is fitting that his work be fully considered before proceeding to a discussion of my own.

## Critical Review

Gil y Gil states that the lethal dose of mercuric chloride for rabbits may be determined from the experimental results of Suzuki (3), Barbour (4) and Nakata (5). He says: "Der erste (Suzuki) dieser Autoren stellte fest, das bei Injektion von 0.003 g. Sublimat bei einem Kaninchen von 700 g Gewicht nach 36 Stunden der Tod eintritt. Ein anderes Kaninchen von 1700 g Gewitcht, welches von Suzuki mit 0.005 g Sublimat auch subkutan injiziert wurde, ging nach 3 Tagen zugrunde. Der zweite Autor (Barbour) bezeichnete die tödliche Dosis mit 0.004 g Sublimat subkutan per Kilogramm Körpergewicht des Versuchstieres.

Auf Grund dieser Resultate bezeichnen wir für 2 kg Körpergewicht eines Kaninchens die mittleren der beiden (0.003 und 0.004 g) Dosen gleich 0.0035 g Sublimat subkutan injiziert als tödliche Dosis." (p. 642)

Reference to these publications shows little basis for such assertions.

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Two animals constitute too small a series on which to base definite conclusions regarding the lethal dose of a poison. Furthermore Gil y Gil overlooked an important complicating factor. The smaller rabbit had intravenously 5 cubic centimeters of carmine and the larger animal 7 cubic centimeters of the dye after the sublimate injection. Suzuki's protocols show that the former died shortly after the carmine injection and that the latter became so weak within four hours that it was killed. The relatively sudden exitus strongly suggests an embolic death. In my experience the injection of such quantities of carmine has more than once been the cause of death in poisoned rabbits. Forbus (6) has likewise found that rabbits are invariably killed by large injections of carmine. Granting that Suzuki may have been more fortunate than others in this respect the fact remains that a complicating factor was introduced and one cannot be certain whether death was caused by the mercury or the dye.

Barbour's sole purpose was to test the efficacy of an antidote for mercuric chloride. Furthermore he introduced the poison intravenously instead of subcutaneously and the doses were based on 1 kilogram body weight rather than 2 kilos as given in the passage quoted.

Nakata's study was primarily concerned with the pathologic stages of the sublimate kidney in the human. For the purpose of comparison rabbits were given sublimate in quantities corresponding according to body weight with that taken by the human cases. In most instances the dosage in rabbits was considerably greater than 0.0035 gm. per kilogram of body weight.

Gil y Gil did not himself study the pathologic changes in the acute sublimate kidney but quotes the descriptions of Suzuki who found in two rabbits after subcutaneous administration of 0.003 and 0.006 gm of sublimate a well marked necrosis of epithelium in the distal and transitional segments of the proximal convoluted tubules. He emphasizes that the amounts capable of producing such damage were administered subcutaneously and that he has given much larger doses intravenously to nearly all rabbits in his series.

The conclusion that renal immunity to mercuric chloride may be experimentally demonstrated is based on the study of nine rabbits. No definite plan of experimental procedure was followed with the exception of time intervals between injections. The irregular manner in which all animals were given both subcutaneous and intravenous injections renders difficult any reliable interpretation of results. Further important information may be gained from the discussion of the microscopic findings in each animal:

Rabbit 1. Necrosis of all except first part of proximal convoluted tubular epithelium; no increase in connective tissue. The author rightfully does not claim that immunity was shown in this case.

Rabbit 2. No demonstrable changes in any tubular cells; hyperemia of glomeruli; glomerular epithelium uninjured. Gil y Gil seeks to explain the marked difference in the kidney of

this animal and the first on the ground that Rabbit 1 received more sublimate in the first two injections than did the second animal. That Rabbit 2 subsequently had a greater amount of poison intravenously without exhibiting kidney lesions led to the conclusion that it was immunized by the first injection since the quantity given was sufficient to produce definite changes in a non-immunized kidney. Here Gil y Gil has quite overlooked such factors as individual differences in susceptibility, variation in absorption of the poison and the fact that the kidney of Rabbit 2 was not examined until twenty days after the last injection, while in the first animal the kidneys were studied two days after the final administration of sublimate. In Rabbit 2 there is no mention of epithelial regeneration yet the animal was considered to be immunized. Again, as in the uranium series, the author fails to state what epithelium becomes resistant. After quoting Menten (7) to the effect that exceedingly small doses of sublimate will produce definite histological alterations in kidney cells within five minutes after injection Gil y Gil allowed twenty days to elapse following an intravenous injection, after which according to his own statement there is rapid and extensive damage, and then considers the kidney immunized.

Rabbit 3. Atrophy of both glomeruli and tubuli in outer zone of cortex; proximal convoluted tubular epithelium well preserved except in some of the third segments where there is obvious necrosis; abundant connective tissue in transitional parts of the proximal convoluted tubules at the junction of cortex and medulla. In this case also Gil y Gil overlooked the very important factor of time. The last sublimate was administered fifty-two days before death and it is highly probable that all of the poison would be excreted long before this time. A poison cannot be assumed to act indefinitely and if cell injury is taken as a criterion of lack of immunity the examination must be made when the injury is at its height.

Rabbit 4. Discussion is unnecessary in this instance since the author does not assert that immunity was produced.

Rabbit 5. Atrophy of cortex with great diminution of epithelium in proximal convoluted tubules which are lined by endothelial-like cells. Most transitional segments of these tubules are difficult to distinguish but appear to have flattened epithelial linings. Evidently Gil y Gil considered this animal immune because of its ability to excrete within three hours about one-third of the last dose of sublimate. The fifteen day interval between the final injection and death is certainly too great for any microscopic evidence of immunity to be of value.

Rabbit 6. Glomeruli unchanged. All tubules intact except the distal divisions of the proximal convoluted tubules where there is cellular regeneration and only slight evidence of injury. Immunity is not mentioned. The protocol shows that the animal lived seventeen days after the last injection and this alone is sufficient to exclude it on the ground that ample

time was allowed for complete cellular regeneration.

Rabbit 7. Fresh degenerative changes in the epithelium generally. The quantitative estimation of mercury excreted after the last injection of 0.01 gm. gave 0.005 gm. and for this reason the kidney was believed to be immunized. This in spite of the microscopic evidence of widespread cellular damage.

Rabbit 8. First and second divisions of proximal convoluted tubules uninjured, some necrosis in distal division. Following the final injection of 0.05 gm. between 0.0042 and 0.0045 gm. was excreted in the urine during the first three hours and the kidney was therefore believed to be immune. When we remember that the selective action of mercury is in the segments of the proximal convoluted tubules, in which the author has described necrosis, it is difficult to believe that any immunity was shown in this instance.

Rabbit 9. No claim is made for immunity.

The author does not state whether or not the intestine was examined in any of the animals. The stain for hyaline droplet degeneration was done in but one instance and was negative.

In order to compare the excretory ability of the kidney in non-immunized and immunized sublimate animals a normal rabbit was given 0.005 gm. of mercuric chloride subcutaneously and the urine collected by catheter for eight hours. In the first four hours there was no excretion while in the second period 0.001 gm. was excreted. From this the author concludes that in non-immunized animal the rate and quantity of excretion is appreciably decreased. However if we compare this result with those obtained in the so-called immune animals it will be found that: Rabbit 5 given 0.01 gm. intravenously excreted about one-third of this amount in three hours; Rabbit 7, with 0.01 gm. subcutaneously excreted one-half the dose, but not until twenty-four hours had elapsed, while in Rabbit 8 which had received 0.05 gm. subcutaneously excreted only about one-eleventh of this amount within three hours. Comparative results are of value only when the dosage and time have been identical.

In summary Gil y Gil states that the experimental results with sublimate corroborate those obtained with uranium. With sublimate it was also possible to build up a remarkable resistance of the tubular apparatus by reason of which the poisons will be, in contrast to non-immunized animals, excreted more rapidly and in greater quantities.

It is obvious that not a single case is convincing and above criticism. In the few instances where immunity was possible the results are questionable on account of the long periods of time elapsing between the last administration of sublimate and the examination of the kidney. The quantatative analyses are of little value as proof of immunity for reasons pointed out above.

### Author's Experiments

In view of Gil y Gil's failure to determine the lethal dose of sublimate and his error in its computation from the work of others it was deemed necessary to establish this point before

proceeding with the immunization experiments.

1. Subcutaneous Lethal Dose

Rabbits of equal weight were grouped in pairs and to each pair the same quantity of poison was administered. The dosage per kilogram of body weight varied from 0.002 gm. to 0.02 gm. Of the fourteen animals receiving from 0.002 to 0.005 gm. per kilo four died (28.5 per cent). These occurred as follows: 0.002 gm. one (17 days), 0.003 gm., two (7 and 8 days), 0.005 gm. one (9 days). The percentage of mortality is not great enough to consider any of these amounts the minimum lethal dose. All of the eight rabbits receiving from 0.006 to 0.012 gm. per kilo survived. Two animals given 0.015 gm. per kilo and one having 0.02 gm. on the same basis died within 2 1-2 to 4 days. The first figure corresponds very closely to that of Lyon (8) who found that 0.0164 gm. per kilo usually proved fatal within twenty-four hours. On the basis of these results 0.015 gm. per kilo has been taken as the subcutaneous minimum lethal dose of mercuric chloride for rabbits.

2. Intravenous Lethal Dose

The same general plan of the subcutaneous group was followed. Seven animals received 0.001 gm. per kilo; six survived, one died after 17 days. Two rabbits had 0.002 gm. per kilogram; one died within 3 days, the other survived. Both animals given 0.003 gm. per kilo succumbed, one after 15 hours, the other in 9 days. So far as is permissible to draw conclusions from the limited number of these experiments 0.003 gm. per kilo intravenously seems to be the minimum amount that will kill all animals. It will be noted that this is exactly one-fifth the subcutaneous lethal dose.

Immunization Experiments

*Material and methods*

Rabbits were used exclusively. The strength of mercuric chloride solution employed was at first 0.001 or 0.002 gm. per cubic centimeter of distilled water. As the dosage was increased the concentration was raised to 0.01 gm. per cc. in order to avoid the injection of such large quantities of fluid as would have been required had the weaker solutions been used.

The subcutaneous immunization series consisted of two groups of three animals each; in one the initial dose was 0.002 gm. per kilo, in the other 0.003 gm. Five rabbits had intravenous injections exclusively, the initial dose of 0.001 gm. per kilo being doubled thereafter. In addition nine animals which had been given sublimate subcutaneously to determine the lethal dose but which failed to succumb were afterward given one or more intravenous administrations.

Intravital staining with carmine, to determine the localization of the sublimate lesions in the tubules, was carried out in one acute and one chronic sublimate animal.

*The acute mercuric chloride kidney*

In none of the kidneys of animals dying from the effects of small subcutaneous doses of mercuric chloride was there any appreciable necrosis of

tubular epithelium. Three were studied, seven, nine and seventeen days respectively, after administration of the poison. All showed high grade parenchymatous degeneration of the tubular epithelium but little actual necrosis. In the glomeruli aside from slight swelling and sometimes desquamation of epithelium covering the tufts nothing was observed except congestion of the vessels.

With higher dosages (0.015-0.02 gm.) definite necrosis of cells in the distal and transitional segments of the proximal convoluted tubules occurred. The affected segments are found here and there in all zones of the cortex with many still escaping injury. At this stage (2 1-2 to 4 days) practically all cells in the divisions affected by the sublimate are dead, for the most part desquamated, and forming loose casts at the site of injury and in the upper part of the descending limb of Henle. The few nuclei still present are markedly pyknotic. A distinct difference is noted in the appearance of some of the dead cells in the mercury kidney from that seen in the uranium organ in that their morphology is fairly well preserved and the cytoplasm has a distinctly hyaline appearance. Most cells however break up into finely granular debris. Fat in the necrotic cells is less constant than in uranium nephritis. The epithelium of the first and second divisions of the proximal convoluted tubules shows parenchymatous degeneration. The glomerular vessels are moderately congested; no apparent change is visible in the epithelium of Bowman's capsule, but not infrequently the covering epithelium of the tufts desquamates. In the capsular space some albumin is often present but blood is rarely seen. Cystic intraglomerular hemorrhages, so common in the acute uranium kidney, occurred in only three of the thirty six cases studied. Two of the three animals had received large intravenous injections of sublimate. Hyaline droplet degeneration, also common in the uranium kidney, was rarely observed in the acute stages although in one animal having 2 milligrams of mercuric chloride intravenously these bodies were fully as abundant as in any acute uranium kidney. All others were negative. In the tubular epithelium this form of degeneration was noted in five instances where death occurred in the acute stage of poisoning. Calcification of casts was observed in three of twelve rabbits dying from the effects of the first injection, the earliest appearance being the fourth day.

*Regeneration of epithelium*

This begins rather constantly on the fourth day. The new cells are in all respects similar in appearance to those found in the uranium kidney, namely, elongated flattened cells with hyperchromatic nuclei and bluish-pink staining cytoplasm. One important difference is however not uncommon; in the uranium kidney most of the dead cells quickly break up and form granular masses which are soon swept out of the tubules but in the sublimate kidney, not a few cells undergo a hyaline change and remain in the lumen of the affected segments. Often such cells are still present when regeneration begins and the protoplasm of the new cells quickly pushes between the dead

masses and within a short time completely envelopes them. Heineke (9) in a study of sublimate lesions in the human kidney has described in much detail the apparent phagocytosis of dead cells by regenerating epithelium. His excellent plates show exactly the same process I have frequently observed in rabbits. The fate of the new epithelium in such a location is of interest. When the number of dead cells enveloped by new epithelium is not large the tubule may again become patent but when the number is so great as to fill the lumen and these become surrounded by regenerated cells the entire mass may calcify. As the regenerated epithelium in the sublimate kidney grows older it not infrequently becomes somewhat cuboidal but never regains the normal shape and, as in the uranium kidney, always stains darker than the original epithelium and is easily recognized.

### Immunization with Sublimate —General Considerations

For reasons already pointed out in the critical review it was not deemed advisable to duplicate exactly the experimental procedure of Gil y Gil. Instead the general plan by which good results were obtained in the uranium series was followed, i.e., adherence to one mode of administration, allowing sufficient time for epithelial regeneration and as complete a recovery of the animals as possible after each injection. Likewise the same criterion of cellular resistance discussed in detail in my previous paper (1), lack of injury to regenerated epithelium after administration of larger quantities of poison than that known to be capable of destroying the original cells, was used. No cases dying within a few minutes after injection or living long enough after the final dose for regeneration to take place are included. The number of animals meeting these requirements is very small.

It is difficult to conceive of a nephrotoxic substance less well suited for the demonstration of local cellular immunity than mercuric chloride. First, there is almost invariably a marked local inflammation and necrosis of tissue at the site of subcutaneous injections. This must mean that some of the poison is not absorbed and is a very undesirable factor when the full effect is wanted in the kidney. Second, intravenous injection of even moderate sized doses is dangerous. A number of animals in the writer's series died from thrombosis of the right ventricle almost immediately after the larger intravenous injections. In these animals the time which the sublimate could have acted on the kidney was so short that no definite fresh epithelial damage could be made out and for this reason it was necessary to exclude several animals from the immune series. Third, any appreciable quantity of mercuric chloride, whether administered subcutaneously or intravenously, produces in rabbits a marked diphtheritic enterocolitis, so severe that clinically the animals seemed to suffer as much from the intestinal lesions as the nephritis. Furthermore an enterocolitis indicates that the metal is excreted through the bowel as well as the kidney and one cannot be certain how much has reached the latter. Fourth, absorption of sublimate after subcutaneous admin-

istration may be very slight if the degree of kidney damage is a reliable criterion. This is particularly well illustrated by one of the rabbits in the writer's series. The animal received 0.004, 0.008, 0.016, and 0.032 gm. of sublimate over a period of 63 days and was killed 3 days after the last injection. Examination of the kidney revealed only a few tubules with regenerated epithelium; for the most part there was only well marked parenchymatous degeneration and but little actual necrosis. The marked local reaction at the sites of injection and the extensive intestinal lesions found at autopsy in this rabbit were much more severe than those in the kidney. In contrast to this and indicating further the variability in absorption of sublimate may be mentioned the finding of a definite chronic nephritis in another rabbit of the same group which had almost the same quantity of sublimate.

The numerous and serious objections to sublimate just cited makes it impossible to speak with certainty of an acquired immunity of renal cells for this substance. The findings in a few animals in which immunity is possible may now be discussed.

RABBIT 2. 0.002-S

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 9-21-26 | wt. | 1200 | gms. | given | 0.002 | gm. | $HgCl_2$ per kilo subcut. | 0.0024 | gm. |
| 10-21-26 | " | 1490 | " | " | double | initial | dose " | 0.0048 | " |
| 11-22-26 | " | 1800 | " | " | " | second | " " | 0.0096 | " |
| 12-13-26 | " | 1990 | " | " | " | third | " " | 0.0192 | " |
| 1- 3-27 | " | 2040 | " | " | " | fourth | " " | 0.04 | " |

104 days.

Died 3 days after last injection. Total 107 days.

AUTOPSY

Weight 1650 gms. Dry gangrene at site of fourth injection. No ascites or hydrothorax. Marked diphtheritic colitis.

Kidneys: combined weight 20 gms. The capsules strip with slight difficulty exposing cortical surfaces which are in general pale but show also moderate numbers of petechiæ. The surfaces are smooth in places, finely granular in others. On sectioning considerable resistance is encountered but there is no gross evidence of lime salt deposition. The cortex is pale and at the junction with the medulla there is slight scarring.

MICROSCOPIC

Zenker-formalin fixation, hemotoxylin and eosin stain. When the number of proximal convoluted tubules showing recent necrosis of epithelium are compared with the same tubules lined by regenerated cells it is apparent that more damage has resulted from the last dose than all previous ones combined. The lumina of the segments last damaged are packed with desquamated necrotic cells. Regeneration has not yet begun. Casts are very numerous in the Henle's tubules and collecting ducts. None of the casts contain lime salts. In the cortical zone nearest the medulla many of the transitional divisions of proximal convoluted tubules are lined by regenerated epithelium but this is true to a much lesser extent in the intermediate and outer zones of the cortex. The new cells are flattened or irregular in outline with dark bluish-pink staining cytoplasm and hyperchromatic nuclei and often forming giant cells or containing in the cytoplasm the remains of dead epithelium. In some instances the pinkish-staining debris is disappearing leaving large vacuoles which may contain finely granular brownish pigment. The regenerated cells show no evidence of injury. Sections stained for fat with Scharlach-R disclose a considerable fatty content in casts

and some desquamated cells. Some of the cells of the proximal convoluted tubules retaining the original epithelium give the staining reaction for hyaline droplet degeneration.

Glomeruli: Most of these structures exhibit little change except slight loss of epithelium over the loops and more rarely Bowman's membrane. The blood content varies greatly. In all sections there may be seen one or more glomeruli which have been partially destroyed by intraglomerular hemorrhages having the exact appearance of those frequently observed in the acute uranium kidney. The petechiæ seen grossly on the cortical surface are no doubt the rather numerous pure blood casts in the tubules. Hyaline droplet degeneration is fully as pronounced in the glomerular capillary walls, as in any acute uranium kidney. Rarely there is slight proliferation of Bowman's epithelium and still more rarely small epithelial crescents. In this case the glomeruli certainly cannot be regarded as immune but on the contrary are more damaged than usual.

Van Gieson's preparations disclose a very slight increase of connective tissue about the regenerated tubules. In the interstitial tissue are moderate numbers of lymphocytes and plasma cells.

Liver:—slight fatty degenerative infiltration of cells about central veins.

for a few small dark depressions. No difficulty encountered in sectioning, no evidence of calcification. The cortex is pale, the markings are obscured, no fresh necrosis or scarring is visible.

MICROSCOPIC

Proximal convoluted tubules lined by characteristic appearing regenerated epithelium are fairly numerous, particularly in the transitional segments. Although most of the regenerated tubules contain granular debris there is no evidence of injury in the lining epithelium. The convoluted tubules with original epithelium exhibit degenerative changes varying from parenchymatous degeneration to complete necrosis. In some of these are coarse deeply pink-staining droplets which with Mallory's stain take the deep bluish-black color of hyaline droplet degeneration. Regeneration has not yet begun in the last injured divisions of the tubules. Casts of all varieties are abundant. Sections stained with van Gieson's reveal no increase in connective tissue.

Glomeruli: On the whole the vessels are well filled with blood so that the capsular spaces are small. There is no apparent damage to the epithelium covering the tufts or in Bowman's membrane. The stain for hyaline droplet degeneration is negative.

Liver: negative.

RABBIT 2. SUB. II

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 10-16-26 | wt. | 1600 | gm. | given | 0.003 | gm. | $HgCl_2$ per kilo | subcut. | 0.0051 gm. |
| 11- 6-26 | " | 1855 | " | " | double | initial | dose | " | 0.01 " |
| 11-27-26 | " | 1900 | " | " | " | second | " | " | 0.0204 " |
| 12-18-26 | " | 1990 | " | " | " | third | " | " | 0.04 " |

63 days.

Killed 3 days after last injection. Total 66 days.

AUTOPSY

Weight 1765 gms. Ulceration at site of third injection and edema at site of last administration. No ascites or hydrothorax. Bladder contains 10 cubic centimeters of clear yellow urine. Marked diphtheritic colitis.

Kidneys:—combined weight 20 gms. Capsules not adherent, surfaces smooth except

The protocols of a few other rabbits might be added but the degree of immunity attained is not great enough to be of any value.

## DISCUSSION OF RESULTS

Because of the retention of a portion of the mercury at the site of in-

jection and the excretion by way of the intestine it was not considered worth while to attempt to estimate the quantity excreted by the kidney. That part of the last dose in each instance reached the kidney is evidenced by fresh necrosis of original but not the regenerated convoluted tubular cells, indicating increased resistance on the part of the latter. The degree of this resistance is unknown. Had all the last mercury given reached the kidney this would be sixteen times the original dose in the first rabbit and eight times in the second animal, but we know from the intestinal and local lesions that such was not the case.

Tolerance of the whole organism for mercuric chloride is very limited, in most instances being only about twice the subcutaneous lethal dose. This is in marked contrast to the results obtained with uranium for which a tolerance of thirty-two or forty times the lethal dose was frequently attained.

In only one animal in the sublimate series was a truly chronic kidney lesion obtained. The microscopic picture in this instance was very similar to that of a chronic uranium kidney, showing great reduction in the number of original proximal convoluted tubular cells, extensive regeneration, considerable interstitial scarring and pigment deposition in the regenerated cells. The glomerular capsules were thickened, the Bowman's membrane epithelium hyperplastic and forming epithelial crescents and even obliteration of the capsular space. This animal received four intravenous injections, beginning with 0.0018 gm. and ending with 0.0144 gm. Unfortunately death occurred within a few minutes after the last injection, and, although the original epithelium shows parenchymatous degeneration and even early necrosis it was thought advisable to exclude the animal from the immune series because of the short time the poison could have acted. The case is of value, however, to show that sublimate also produces chronic glomerular as well as tubular lesions in spite of the fact that in the acute stage glomerular damage is less constant and less marked than in uranium poisoning. Hyaline droplet degeneration in the glomeruli is not common in either the acute or subacute sublimate kidney, occurring in only seven of the thirty-six animals of the series. In the damaged convoluted tubular epithelium this form of degeneration was observed in twenty-one of the thirty-six kidneys. Fatty degenerative infiltration in living cells and casts was noted in twenty-six instances. In the living cells fat is present in about the same quantity as in the uranium kidney but in less constant and not so abundant in casts.

Fatty degenerative infiltration was observed in the liver only four times, extensive in one, slight in the others. The constant relationship to dosage seen in uranium animals is lacking.

## Conclusions

1. Local corrosive action and irregularity of absorption after subcutaneous administration, the danger of thrombosis following intravenous injection and the excretion by the intestine resulting in severe enterocolitis, makes sublimate an undesirable substance to use in the experimental pro-

duction of immunity in renal epithelium.

2. In rabbits the amount of mercuric chloride absorbed varies greatly. In some several injections may be given without producing any marked change in the renal epithelium while in others the same quantity causes well marked chronic glomerulotubular lesions very similar to those produced by uranium.

3. A slight degree of acquired immunity for sublimate can be demonstrated in regenerated epithelium and glomeruli.

4. Glomerular injury, as evidenced by necrosis of epithelium, hemorrhages and hyaline droplet degeneration is less frequent than in the uranium kidney.

5. A constant and striking phenomenon in the sublimate kidney is the envelopment of necrotic cells by regenerating epithelium.

6. In the rabbit calcium deposition in casts is inconstant.

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# Etiology of Backache in Medical Practice*

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WHEN I was asked to discuss backache from a medical standpoint it was understood that the discussion was to be limited to those aches which are experienced in the lumbar and sacral regions. My remarks will be confined to this locality.

Backache, like headache, fever, and blood pressure is a symptom, and may require considerable investigation on the part of the physician before its cause is ascertained. All of us realize that there are a large number of causes. Fortunately other symptoms are commonly associated with backache which make it appear at once only incidental to the condition. We should always think of backache in this manner. As one limits his practice the importance of his specialty is likely to dominate the etiology, thusly at one time the gynecologist believed most backaches were due to pelvic disorders, the urologist that most were due to kidney diseases, the orthopedists held that they saw a lot of backache from strains, osteal conditions, and malformations of the spine, and we in medicine are sure that most are due to infectious states. No doubt we are all correct, as each sees that which he specializes in and finds backache associated with it.

It is very important that we familiarize ourselves with all of the possibilities that will be mentioned here tonight, and be prepared to make those investigations that are necessary to make a final diagnosis before attempting to institute measures of relief. One should have a workable outline in mind when a case of backache comes to him for solution, and a classification as follows will be helpful: 1st—Backaches from systemic diseases; 2nd—from local conditions, and thirdly: from reflex conditions. Systemic conditions are a reason for the majority of backaches seen in the general practice of medicine, and acute and chronic infectious states hold first rank, with metabolic disorders, coming in for consideration quite frequently. The backache from an acute infection, as tonsillitis, or grippe, is easily recognized. Those due to chronic foci of infection, on the other hand, are sometimes very difficult to locate. Blood diseases, syphilis, and some of the metabolic states as hypothyroidism may require some study before one can say definitely that they are the cause of the backache. After one finds a condition, and it is corrected, it may take some time to prove that it was the cause of the backache. Some of the most stub-

*Internist's discussion of backache in symposium before Cleveland Academy of Medicine, February 1928.

born backaches are frequently cured by the removal of chronically infected teeth, tonsils, and treatment of infected sinuses. After one satisfies himself that there is no possibility of infections or metabolic disease being the cause he should make an investigation of the local factors. These might be sacroiliac strain, positional muscular strain, spondylitis, malposition of the spine, spinal tumors, and anomalies of the vertebrae. Coccyxalgia is often encountered in nervous men and women, and its cause often unexplained. Occasionally one may find an old fracture with pressure on the nerve roots. The most common local causes in my practice have been spondylitis and sacroiliac strain. Sciatica is a common finding due to arthritis. This used to be seen more frequently. It is probably decreasing due to more thorough eradication of foci of infection. The few local causes given are not a complete list. Among the reflex states pelvic diseases, prostatitis, hemorrhoids, renal calculi, pyelitis, acute and chronic intestinal infections, and over sexual indulgence should be thought of. Over sexual indulgence probably produces backache from pelvic congestion as does menstruation. Often the back aches periodically from mental and physical fatigue, and there is a psychoneurotic backache.

The following is a table of 104 cases of backache clinically studied, which shows the relative frequency of a number of the causes discussed above:

CAUSES OF BACKACHE

| 1. *Systemic Conditions*: | Cases |
|---|---|
| A. Chronic foci (with its myositis and neuritis | 23 |
| B. Arthritis deformans | 12 |
| C. Hypothyroidism | 6 |
| D. Hyperthyroidism | 4 |
| E. Psychoneurosis | 4 |
| F. Acute indigestion | 3 |
| G. Acute infections | 3 |
| H. Chronic nephritis | 2 |
| I. Periodic fatigue, postural strain, and flat feet | 2 |
| J. Orthostatic albuminuria | 1 |
| Total | 60 |

| 2. *Reflex Conditions*: | Cases |
|---|---|
| A. Chronic appendicitis | 5 |
| B. Gall stones | 3 |
| C. Spastic constipation | 3 |
| D. Renal calculus | 3 |
| E. Congestive pelvis | 3 |
| F. Retroperitoneal glands | 2 |
| G. Abdominal ptosis | 2 |
| H. Retrodisplaced uterus | 2 |
| I. Mucous colitis | 1 |
| J. Carcinoma of rectum | 1 |
| K. Pregnancy | 1 |
| L. Uterine fibroid | 1 |
| M. Ovarian cyst | 1 |
| N. Prostatic hypertrophy | 1 |
| O. Labial hernia | 1 |
| P. Renal ptosis | 1 |
| Total | 31 |

| 3. *Local Conditions*: | Cases |
|---|---|
| A. Radiculitis | 2 |
| B. Sacroiliac strain | 6 |
| C. Lumbar neuralgia | 3 |
| D. Coccyxalgia | 1 |
| E. Anomaly of fifth lumbar vertebra | 1 |
| | 13 |
| Total | 13 |

We feel that an outline of some of the factors mentioned above will be of value in the study of backache, and the answer to the cause of most cases seen will be found in the list mentioned. Time will not permit me to speak of the methods of diagnosing all of the conditions stated, but a few remarks on examination of the patient will be given.

The patient examined for pains in the lower part of the back should be completely undressed, and the posture carefully noted. Often round shoulders, protuberant abdomen, and the relaxed condition of the musculature will be valuable points. The lordotic back should always be looked for. The tension of the muscles over the lumbar region should be noted, as here resides most pains from infections and strains. A careful palpation of the sacroiliac joints and lumbar nerves should be made. Valuable information can be obtained by deep abdominal palpation with thoroughly relaxed abdomen. In a properly relaxed patient firm pressure through the abdomen will locate sensitive nerves which cannot be located otherwise. While making this examination a floating kidney, or chronic appendix can be recognized. A pelvic examination will give information regarding tumors, and position of the uterus. Infections of the adnexa may be discovered. An examination of the prostate in the male, and sometimes its secretions for evidence of chronic infection may be necessary. One should not neglect to make an examination of the rectum for tumors and hemorrhoids. In many cases it is necessary to make radiographs of the teeth and sinuses. A careful examination should be made of the tonsils. It is important to know the condition of the arterial and respiratory systems, as conditions therein may be the sources of infection or chronic fatigued states. A urine examination should not be neglected, as often microscopic blood or pus may give a clue to the cause. Some of the local causes of backache are not discovered until an X-ray examination is made with a Bucky diaphragm. We have had three cases of calcified retroperitoneal glands which were tender on palpation through a relaxed abdomen that would have escaped discovery without the assistance of the X-ray. It can readily be seen by the remarks on physical examination that it must be thoroughly done. One should not haphazardly have all the examinations made which have been mentioned, but should judge which studies are necessary after the physical examination. One who makes a diagnosis of backache from X-ray or local examination may be misled. In no field of medicine is the knowledge of diagnosis so necessary. Root pains of luetic crisis, diabetic neuritis, myelogenous leukemia, and osteitis deformans (Paget's disease) are some of the causes that I have seen of backache. Sharp shooting pains occurring every day at about the same time, or with change of position, coming on and remaining for two or three weeks at a time, and then disappearing without any apparent reason, may be radiculitis. I have seen two such patients, and one has had this condition of affairs for forty years. The urologist sometimes surprises you by what he finds by pyelography.

The reason why the cause of backache is not discovered more often is on account of the lethargy of ourselves. We realize that it is not often serious, and do not investigate thoroughly. There is no doubt that this symptom interferes with the welfare of almost as many people as does headache, and it should not be neglected. About one-tenth of our patients who are studied for chronic disease complain of backache.

# Observations on the Coincidence of Endocrine Dystrophies and Mental Subnormalities*

By William G. Downs, Jr., *Department of Anatomy, College of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania*

SINCE the now famous reports of Brown-Sequards on the results of testicular injections and transplants, and the ensuing work of other less well-known and imaginative observers, almost every effect which might be conceived, has been attributed to the glands of internal secretion. Many of these apparent results have seemed to be well-substantiated, while many are quite obviously merely the offspring of the purest flights of imagination. Because of this latter rather awe-inspiring group the more serious students of the field only essay new attacks upon endocrine problems with the greatest diffidence, and consequently many extremely fruitful lines of investigation are left wholly or nearly untouched. In the following observations I have attempted to keep as close to demonstrable fact, based upon careful analysis or experimentation as possible, yet the implications are such that one can scarcely resist the temptation to, to some extent, speculate upon the possibilities divulged. Much of what I wish to submit is only in the nature of hypothesis, and until further and more conclusive studies can be made, is not to be accepted as in any sense final.

Endocrine dyscrasias occur with such frequency among groups of mental defectives that even the most chance observer is struck with the significance of it.

While marked endocrine types are relatively infrequent among the population at large, a very great per cent of the patients in any institution for the care of mental defectives display unmistakably the symptoms of endocrine defects. It is only to be expected that if the glands of internal secretion have any effect whatever upon the organism, such a delicate and nicely-balanced mechanism as the central nervous system cannot help but be involved. Whether this is actually what does take place, or whether the endocrine dystrophy and the changes in the central nervous system are, alike, the result of some more obscure etiology, possibly of a genetic nature, is yet to be proved. That certain parallels of this character do occur is evident, and there is ample experimental evidence to warrant the belief that changes in the glands alone are adequate to bring them about. The studies of Lipschütz, Moore, Myers, Sand and others upon the male sex-glands following castra-

*Read before the section on Sanitary and Medical Sciences of the Michigan Academy of Sciences, Arts and Letters at Ann Arbor, March 30, 1928. This study was completed while the author was a member of the staff of the Dept. of Anatomy, University of Michigan.

tion and vasectomy prove beyond question the power which these glands, at least, have in influencing psychic development and change. Other equally convincing evidence has been submitted by Cushing, Dercum, Kanavel, Goetsch and others as regards the pituitary, while the psychic relationship of thyroid and pancreas has become so well-known as to require no further comment.

It is quite true that our knowledge of symptom-complexes is not yet adequate to enable us to definitely fix upon the exact gland or glands involved in many cases. It is equally true that while a single gland may be primarily involved in many instances, these manifestations are invariably to be attributed to a derangement in varying degree and proportion, of the whole endocrine system. For this reason it should always be borne in mind that when we speak of the thyroid as the causative factor in a given condition, or the hypophysis, or the testes, we mean that the single gland mentioned is apparently of primary importance, but that other glands are likewise involved, very possibly as causative factors. Among these groups are especially those cases classed as mongols, traceable apparently to thyroid dysfunction, cretins, which I believe are, basic to the thyroid disturbance, of hypophyseal origin, and the various gonadal dysfunctions. Of these groups, the first two at least, and the last, probably, in addition to the physical variations which make possible the diagnosis, each falls within a fairly definite range of mental development, which appears likely to prove as definitely symptomatic as is the physical complex.

In a series of twenty-one cretins which I examined, after eliminating those cases of a distinctly debatable type, I found the intelligence quotient of these patients to vary between the limits of 35 and 65 (Binet). On the whole, the average for this group was somewhat nearer the higher limit. The cases of mongolism, of which 38 were examined, were of a definitely lower order, their range being between an I.Q. of 15 and 45 and the average tending toward the lower limit. In addition to their falling into what may be accused of being a somewhat academic grouping, each individual of each of these types evidenced a considerable number of reflex actions which are not far from identical for all of those patients grouped within the class. Further than this is the notable fact that their responses given to the tests used to ascertain the mental age were very similar for all of the individuals falling within a given diagnostic group. That is, cretins will not only show an I.Q. within the designated limits for their group, but their responses to the various parts of the tests will be very closely similar for all. The same statement applies with equal force to mongols, and insofar as one is able to group them into fairly definite endocrine classes, to the parathyroid dystrophies, adrenal dystrophies and possibly other groups even less definitely classifiable.

It is in the class of sex-gland dystrophies that some of the most surprising results are obtained. One would expect, I believe, that precocious

sexual development would go hand in hand with a more advanced mental state and expect delayed pubescence to be coincident with retarded mental development. Such I did not find to be the case. The closely allied types of mental responses do not hold good in these cases, but on the whole, the delayed sex-development cases show a considerably higher I.Q. than do those having a pathologically advanced stage of sexual development. It is highly possible that the variation in response type may in these cases be due to their having different etiologies. One may have advanced puberty arising as the result of pituitary, adrenal or gonadal dystrophy certainly, thymic dystrophy probably, and it is not unlikely that such conditions may arise from the dysfunction of still other glands. In addition to this possibility is the one that many such cases may be the result of combinations of such dystrophies. I am inclined to think that were it possible to segregate these cases into definite types according to their distinctive etiology, it would be found that their mental status would be just as clearly limited as appears to be the case with the other more sharply outlined types of endocrine cases. One does find that the familiar "fat-boy" type, which is probably of hypophyseal origin, in addition to his delayed sexual development, has a fairly high, if somewhat sluggish type of mentality, while the late adrenal group of overdevelopment is inclined to be mentally rather inferior. I am not considering here those cases of precocity having their origin in adrenal tumors. The possible mechanism of their operation is considerably involved and much depends upon the time at which such cases are seen If viewed early they are apt to appear rather precocious, while later, mental changes of a decided retrogressive nature make their appearance and run a relatively rapid course. Eunuchoidism also exhibits a wide range of results due to the equally wide range of causes. One would expect the loss of ambition resultant from a loss of libido to throw these cases into an apparently retarded group. Apparently this is frequently true, true possibly in an, as yet, undifferentiated type of cases. On the other hand, it is frequently true that an apparent freedom from the distractions of sex-impulses releases mental energy which presages rather marked advancement. These apparently conflicting results may very possibly be due to the etiological factor concerned. One cannot always say with certainty that a eunuchoid case is definitely a gonadal dystrophy. It may be hypophyseal, thymic, epiphyseal, or adrenal in its origin or may be the result of a combination of these factors. Were it possible to always place it as being definitely one or the other, I suspect that we should find the mental status quite as characteristic as any of the physical signs. Experimental evidence from the lower animals and that from the study of human castrates would certainly tend to support this view.

Affections of the female sex-glands unquestionably have extremely far-reaching and important psychic effects. The high rate of mental disturbances coincident with the onset of puberty and with the climacteric is in itself evidence of this, as are the disturbances so often found following

castration in the female. The exact relationship existing between the ovaries and mental deficiencies is not clear. It is surprisingly true that the hermaphroditic type of female frequently appears to possess a marked libido with very little or no restraint. This is probably not a true libido, but is due to a coincident greater aggressiveness, rather than to other causes. The frequent tendency of these cases toward homosexuality would tend to bear out this belief. On the whole, my observations upon female defectives would lead me to believe that generally, the lower the mental type, the weaker is the libido in a given individual. In many ways, the other possible effects of the ovaries upon the psyche parallel closely those of the testes in the male. In both sexes, the statement that a high degree of sexuality is apt to accompany advanced mental attainments and psychic virility may be I think, safely projected. Stockard believes that a great deal of confusion has arisen in judging this subject, due to the fact that what is really a type of exhibitionism—a sort of defense reaction, is frequently mistaken for advanced libido but is really evidence of a low degree of sexuality. I am quite certain that promiscuity is no criterion of sexuality, but is more often merely an evidence of weak mentality.

As additional evidence is advanced which enables us to more accurately mark out the limits of the various hypophyseal dystrophies, these begin to reveal striking and rather characteristic variations. As regards thymic dystrophies, the same situation governs which we find in the gonads. One can never be quite certain where the effect of thymus ends, and that of hypophysis, thyroid, gonads or adrenals begins. As for the pancreas, the mental characteristics of advanced pancreatic diabetes are familiar to all, as is probably the fact that there is a distinct line of demarcation between pancreatic diabetes and the diabetic conditions of an apparent hypophyseal origin.

While the line between mental subnormality and insanity is a particularly distinct and well-marked one, it has been demonstrated that in many of the dementias, as well as in feeble-mindedness, there is present a well-marked and clear-cut variation from normal in the condition of most of the glands of internal secretion. In such psychopathic cases, which condition takes precedence in either time or etiology, I have not the temerity to suggest. The mere fact of their coincidence, does, it seems to me, carry a definite suggestion when viewed in the light of such effects in other and better known conditions.

In summary, a majority of the endocrine dystrophies present marked and definite psychic symptoms peculiar to their class. It seems probable that both somatic and psychic symptom-complexes are the result of endocrine disturbances, acting upon the entire organism, including also the other glands of internal secretion. It is probable that still deeper than these hormone effects are other more obscure causative factors, which, through the glands of internal secretion, affect the entire organism. It is obvious that the way in which many experimentally produced endocrine variations affect the organism is a close parallel to many

definitely hereditary aberrations. It seems, then, plausible to believe that heredity may in great part function through the medium of the endocrine system, to produce definite symptom-complexes involving both physical and psychic changes of definite and characteristic types. It is to be hoped that such conditions may eventually become so well-recognized as to constitute unmistakable diagnostic syndromes.

I wish to express my indebtedness to Dr. W. J. Kay and the staff of the Michigan Home and Training School for the opportunity to make the studies of which this report is a preliminary, and for their very cordial and wholehearted cooperation in the work involved.

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# A Case of Glioma of the Centrum Semiovale of the Right Parietal Lobe

By Hermon C. Gordinier, A.M., M.D., F.A.C.P., *Troy, New York*

TUMORS involving the white matter of the parietal lobe are not common, and relatively rare are those of an infiltrating type that involve by direct pressure or actual destruction the sensory or motor neurons of the corona radiata or internal capsule.

The case of tumor herein recorded, therefore, is interesting because its location and growth was such that it gradually involved by pressure and ingrowth the fibers of the foot of the corona radiata and those of the posterior part of the dorsal limb of the right internal capsule. It implicated in a most selective manner the thalamocortical sensory path, affecting at first the sensory neurons conducting sensations of position, muscle sense, stereognosis and thermal sense, and caused complete left sided hemiataxia, loss of the sense of posture, astereognosis and changes in temperature sense. It interfered slightly with those fibers conducting superficial sensations, occasioning but slight diminution of the sense of contact, touch and pain. Later on the right motor path became involved when an incomplete hemiparesis gradually appeared, the left lower extremity being most affected, whereas the left upper extremity, face and tongue were only slightly involved. The position of the growth was such in relation to the dorsal limb of the right internal capsule that it did not compromise the fibers of the right optic path or radiation as at no time was hemianopsia detected.

*Case Report.* Mr. F. H., age 52 years, entered the Mary McClellan Hospital October 23, 1921, complaining of great weakness, frontal headaches, inability to concentrate and numbness of the whole left side, which clinical manifestations have been coming on gradually but increasing in severity over a period of about six months.

*Family History.* Both father and mother are living and in perfect health. Two brothers are well, none dead. No nervous, mental or hereditary diseases are recorded in the family. His wife is healthy, she has two healthy daughters, and no still born children or miscarriages.

*Previous History.* The patient is a banker of rather sedentary habits but a very hard worker. His hours have been long and he has had no vacation in many years. He has had the usual diseases of childhood, remembers no serious complications. At six years of age, he was very ill with pneumonia, otherwise until the onset of the previous illness, he has been in good health. Since a boy he has been a sufferer from hay fever. Recently he put on glasses to overcome floating specks before his eyes. He has suffered from no accidents or injuries nor has he had any surgical intervention. He has had no sore throat, his appetite is good, has no digestive disturbances but is a little constipated. He has no nausea or vomiting. He sleeps poorly and has lost five pounds in weight. He states that he never had a venereal infection.

*Present Illness.* For the past six months, Mr. H. has tired easily and is very easily fatigued. He developed at first numbness in the left leg and later in the left arm. At first the numbness was only noticed at night; it would often awaken him and after urinating, relief would frequently come and he would then fall asleep. He suffers from no pain in the leg or arm. He now has a poor appetite. Tobacco and food do not taste good and he feels quite tired out. Neither he nor his friends have noticed the slight flattening of the left side of his face.

*Physical Examination.* General: He is a well developed, well nourished man past middle age. Color, pale. Rather listless and apparently disinterested in life.

Head: No tender areas about skull. Eyes react normally. Extra ocular movements are normal. Eye grounds are negative except for rather small slightly tortuous vessels. Ears and nose are negative. Teeth—several badly carious. Throat clear, tonsils small.

S.L.N.: Neck flexible. Lymph glands not enlarged. Thyroid glands not palpable.

Skin: Many small scattered angiomata on trunk. Also some small yellowish slightly raised and roughened lesions that look like lesions of psoriasis, though they are not.

Chest: Heart, regular, good quality of sounds. No murmurs or enlargement. Pulse good quality and equal. Bl.P. 140/85. Lungs resonant throughout. Good expansion. No adventitious sounds. Normal breath and voice sounds.

Abdomen: Normal contour. No tenderness or masses. Inguinal rings normal.

Genitalia: Normal.

Rectal: Prostate of moderate size, normal consistency, but seems tender. There is a thickened fold of mucus membrane just inside the anus.

Extremities: No edema or deformity.

*Neurological Findings.* Cranial Nerves. Pupils are of medium size, equal and reactive to light and accommodation. No ptosis or diplopia. The extraocular excursions are normal. There is no constriction of the visual fields and no hemianopsia. The discs and retinae appear perfectly normal, the vessels are rather small and tortuous. The sense of taste and smell and hearing are normal, and no difficulty exists in swallowing. There are no evidences of dysarthria, aphasia or agraphia. His mind is clear although the reaction time is decidedly prolonged. When questioned, his answers are long delayed but always correct. He is not disoriented or delirious but shows no interest in matters pertaining to his home life or business.

*Motion.* There is distinct flattening of the lower left side of face with partial obliteration of the left nasolabial fold, the muscles innervated by the motor division of the left fifth nerve are not involved. The tongue deviates distinctly to the right. There is slight weakness of the muscles of the left arm, hand and leg as compared with those of the right side. There is no atrophy or tremor. The gait is unsteady and there is definite circumduction and dragging of the left leg and foot. When tested for Romberg, there is definite swaying toward the paretic side due to weakness of the left lower extremity.

*Sensation.* The finger to nose and heel to knee tests bring out marked ataxia of the left upper and lower extremity. The sense of position is lost in both left arm and leg. There is complete astereognosis of the left hand, with the eyes closed numerous test objects placed in the left hand are not recognized. Light touch is diminished over the left arm, leg and foot, and there is a small area just above the ankle on the under side of the leg where tactile sense is lost. Thermal sense is decidedly diminished over the whole left arm and leg and nowhere absent. There is also hypalgesia over the same named part.

*Reflexes.* The tendo achilles and patella tendon reflexes are decidedly hyperactive on the left side there is no knee or ankle clonus. There is a definite Babinski reflex which is, however, not well sustained. There is no Oppenheim, Gordon or Shattuck reflex present. The triceps and wrist tendon reflexes are lively on the left side. The abdominal and cremasteric reflexes are

1.—Longitudinal section of right cerebral hemisphere showing tumor mass of centrum ovale of right parietal lobe.

2.—Longitudinal section of right cerebral hemisphere showing wedged shaped tumor mass implicating the extreme end of the dorsal limb of the right internal capsule and surrounding white matter of parietal lobe.

3.—High power photomicrograph showing the various types of cells in the tumor. Bipolar spongioblasts. A few larger cells somewhat resembling astrocytes. Stroma much vacuolated.

absent on the left side but present on the right. The organic reflexes are controlled.

*Laboratory Examinations.* R.B.C. 5,330,000, W.B.C. 8,600, Polys. 57%, Lymphos. 43%. Blood Wasserman and spinal fluid negative. Urine examination—Sp. Gr. 1.020, reaction acid, sugar negative, albumin—very faint trace, mucous shreds excess, casts—few, dye test 50% excreted in 1st hour and 10% in 2nd hour, test day—night specimen urine 97 c.c.—1.020, 10 A. M. 74 c.c., 1.019, 12:45 P. M. 91 c.c.—1.011, 3:15 P. M. 120 c.c.—1.010, 5 P. M. 50 c.c.—1.022. Spinal fluid under slightly increased pressure, cells—5 small lymphocytes per cm., globulin x, gold curve showed no change in color.

## Summary of the Subjective Neurological Symptoms and Findings

Six months previous to entrance to hospital, patient began to suffer with at first severe frontal headaches, great general weakness, numbness of left leg and several weeks later numbness of the left arm; this was followed by slight weakness and later paresis of left leg and arm, dragging and circumduction of left lower extremity, slight lower facial and left lingual paralysis. Examination showed slight diminution of tactile but definite diminution of the temperature sense and hypoalgesia of the left arm and leg with definite ataxia and astereognosis; slow cerebration without aphasia, intact cranial nerves, no optic edema or neuritis, negative spinal fluid under slight pressure, with slowly approaching coma and death.

From a careful study of the above

surrounding white matter of parietal lobe.

mentioned subjective symptoms and clinical findings, three diagnostic possibilities seem to present themselves: firstly, a possible syphilitic endarteritis with thrombosis of one of the branches of the right lenticulo-striate artery and consequent softening of the posterior limb of the internal capsule; secondly, a subacute or chronic encephalitis involving the right corpus striatum and optic thalamus; thirdly, and most probably, an infiltrating new growth, located deep in the centrum semiovale of the right parietal lobe, which had by gradual extension and pressure involved either the extreme dorsal limb of the right internal capsule, or the sensory and motor paths of the foot of the corona radiata above and outside of the internal capsule, in view of the absence of left homonymous hemianopia or defect of hearing. As the physical examination showed no stigmata of lues and as both the blood and spinal fluid showed a negative Wasserman reaction, cerebral syphilis seemed excluded. While a subacute or chronic encephalitis is clinically very difficult of exclusion, the slow unilateral progression of all neurologic manifestations, the absence of the characteristic cranial nerve implications of encephalitis, together with continuous frontal headaches, characteristic approach and progression of the sensory and the onset later of the motor manifestations seemed to exclude encephalitis, and despite the absence of optic neuritis, favor the diagnosis of a new growth implicating the sensory and motor neurons of the posterior limb of the right internal capsule or of the right centrum semiovale just above the dorsal limb of the capsule.

10/10/21. Patient remained about as described until the day before his death. Blood pressure then 160/90 and that afternoon he began to show left sided spasticity. The morning of the 9th, he showed greater spasticity with increased deep reflexes. Bl. P. 200/125. Eye grounds showed no changes. At noon he could barely swallow and seemed very dull mentally, gradually passing into a semi-comatose state. At about 2 P.M. the coma was still incomplete, he could be aroused fairly well, although he answered questions very slowly. Cheyne-Stokes respiration appeared and he died of respiratory failure at 1:45 A.M.

### Autopsy

A general autopsy was not allowed, permission, however, was granted to examine the brain. On removal of the calvarium, there was found no bulging or no increase of cerebro-spinal fluid. The dura was free and not especially tense. The brain surface appeared normal as did the Pacchionian bodies; the vessels of the surface and at the base of the brain appeared normal. Deep within the centrum semiovale of the right parietal and most ventral part of the occipital lobe there was an infiltrating new growth, very vascular and the seat of numerous hemorrhages; this growth was irregularly ovoid and extending forward and inward like a wedge and seemed to involve by pressure or extension the extreme end of the posterior limb of the internal capsule, the ventral limb of the capsule appeared perfectly nor-

mal, the corpus striatum or optic thalamus showed no change. Sections through the left hemisphere, crura, pons, cerebellum and oblongata macroscopically appeared normal.

The tumor on section diffusely invaded the surrounding tissue and showed many degenerative changes. The cells of the neoplasm vary a great deal in size, shape and staining properties, many being bipolar and of spongioblast type, others apparently unipolar and still others larger and more of astrocyte type. Mitotic figures are numerous. The stroma consists of the glial processes of the tumor cells and of thickened capillaries which are very numerous. The vessels show marked hyaline change and also adventitial proliferation. Hemorrhage, cystic and anemic degeneration are present in many parts of the growth. The tumor agrees with the usual description of the spongioblastoma multiforme.

# Joseph Rodman Drake, M.D., Physician and Poet

By Lieut. Comdr. Louis H. Roddis, M.C., *U. S. Navy, Washington, D. C.*

On a number of occasions Sir William Osler called attention to the considerable number of physicians who have been eminent as men of letters. The list includes the names of Rabelais, Keats, Crabbe, Goldsmith, Garth, Arbuthnot, Akenside, Sir Thomas Browne, Smollet and Oliver Wendell Holmes. Among the ancient writers is St. Luke whose contribution to the New Testament has been called the most beautiful book of the Bible. Dr. Osler also points out how infrequently distinction has been attained in both medicine and literature, Holmes being the most notable exception, as in addition to taking high rank as a poet and essayist he was a pioneer in bringing surgical asepsis to the child-bed.

Joseph Rodman Drake is one who can scarcely be said to have possessed any unusual measure of merit either in letters or medicine but interest nevertheless attaches to him as a member of our profession who was one of the earliest of American poets to receive recognition in Europe. His brief and not unromantic career, the charm of his personality, the beauty of some of his verse, and the oft quoted elegy of Halleck has led me to bring him to notice in a short sketch.

The poet physician was born in New York City August 7th, 1795. The family had been settled in America since 1630 and several ancestors had taken an honorable part in the Colonial and Revolutionary Wars. The original American ancestor, John Drake, had come from Devonshire and was probably a member of the same branch of the family that had produced Sir Francis Drake, the famous Elizabethan navigator. The early death of his parents left Joseph and his three sisters as orphans of tendor years. His childhood was spent in poverty. It is more than probable that the hardships and deprivations during this period did much to undermine his health and paved the way for the tuberculous infection thât caused his death. He was extremely precocious, a great reader and like many poets was a scribbler of verse almost from the cradle.

His straitened circumstances made it necessary for him to seek employment as soon as possible and when but seventeen he began work as a clerk in a mercantile house, "The sugar and cotton line" of his verse. In the winter of 1812-13 he met Halleck with whom he was to be associated in his literary work and who was to write the famous elegy on the

Joseph Rodman Drake, M.D. (1795-1820)

death of his friend. They lived as young men at the home of Colonel Russell whose cook was celebrated for her succotash. Drake had a distaste for business and in 1814 began the study of medicine with Dr. Bruce and Dr. Romayne, both well known New York physicians of the day. The old preceptorship method of teaching was then a common mode of entering into the profession and it was customary to "read medicine" with a preceptor, accompanying him on many of his calls, and attending and assisting him in his office practice. Drake's medical studies did not hinder him from making many boating and fishing excursions with Halleck, Dr. DeKay, and another fellow student under Drs. Bruce and Romayne, Edgerton Winthrop, a nephew of Mrs. Peter Stuyvesant. Mrs. Stuyvesant's home was in the neighborhood of St. Marks Church with the lawn sloping to the East River and Drake, DeKay, and Halleck were frequently visitors there. A favorite fishing spot for the young men was at Burnt Mill Point, now 10th Street.

The New York of the early 19th century was a picturesque old place, the center of the present metropolis being then miles distant in the country. It was the real capitol and with the growth of the Knickerbocker school of authors of which Drake and Halleck were to be members, it became a rival of Boston as the cultural capitol. The social life was cultivated, gay, and unconventional and the three young medical students took an active part in it. They were frequent visitors in the home of Henry Eckford, a wealthy shipbuilder who lived in a handsome old residence approached by a beautiful shaded drive called Love Lane occupying about the present line of 21st street between 6th and 7th avenues. DeKay and Drake both married daughters of Eckford. Drake had his office at the corner of Park Row and Beekman street in a house that later became his residence. With Langstaff he conducted a drug store in the basement, the firm being known as "Drake and Langstaff." We have no record of Drake's license to practice medicine but the New York Academy of Medicine recently published the copy of a license loaned them by Dr. William S. St. Thomas issued in 1816 to Charles P. Livingston. If we change the names of the licentiate and his preceptor we would no doubt have a duplicate of Drake's license. A copy of the Livingston license is here produced. It was printed and written on a large sheet of very handsome paper.

A License to Practice Medicine in New York State in 1816

We the President and other Officers of the incorporated Medical Society of Dutchess County in the State of New York, having received from our Censors full assurance of the Competent Knowledge of Charles P. Livingston in the theory and practice of Medicine, and from Doctor James Downes his former preceptor the like assurance of his Standing and moral deportment; do by the powers vested in us Confer upon him the said Charles P. Livingston license to practice Physic, Surgery and Midwifery in any part of this State and recommended him to the confidence of our fellow Citizens, and the friendly attention of our brethren as a person of good morals and liberal attainments.

In Testimony whereof we have subscribed these presents with our names, and caused our Seal of Incorporation to be annexed.

Done at Poughkeepsie this Sixteenth day of July 1816.

*Seal* Attest JOHN THOMAS, President.
JOHN BARNES, Secretary

Agreeable to the By-Laws of the Medical Society of the 20th Medical District of the State of Ohio Charles P. Livingston is admitted a Member of Said Society.

ORESTES J. E. HAWLEY, President.

It was at the Beekman Street home that Drake with Halleck wrote the verse satires that appeared in the New York City Post under the title of the Croaker Papers. For a considerable period the authors were unknown even to Coleman the editor of the Post. Most of their work has been forgotten as it owed its popularity largely to local knowledge of characters and circumstances but at the time it attracted wide attention. Our modern "Columnists" are the nearest approach to this type of journalism and are the lineal descendants of the "Croakers."

In 1816 Drake published his best known poem, "The Culprit Fay," and in the same year he married the daughter of Henry Eckford. The impecunious young doctor was at once rasied to a position of relative financial ease. He continued the practice of his profession, but seems to have given most of his time to social and literary activities. He was young, good looking, and a poet, three of the best credentials to any society and to them were added a playful, kindly and affectionate nature that quickly endeared him to associates.

In 1818 he visited Europe with his young wife. His health began to fail after his return and as symptoms of pulmonary disease appeared he was advised to spend the winter months in a milder climate. Drake showed little concern regarding himself and it was with difficulty that he was persuaded to follow a dietary regime or take any regular treatment. He did, however, spend the winter in Lousiana but tuberculosis had gained such headway that after lingering through the following summer growing weaker and weaker he died September 21, 1820, being but 25 years of age. Thus he became one of a great company of youth and genius.

Possessed of some strange spirit of fire,
Quenched by an early death.

Dr. Drake was but a minor poet judged by the verse he left though it was of such a character as to promise greater things. "The Culprit Fay" was his most ambitious effort. It contains little more than six hundred lines and is noteworthy in that for the first time American scenes were considered as worthy of description in verse. The scene of the poem is on the Hudson in the vicinity of West Point, and the following is a fine example of a poetic description of moonlight on mountain and river:

'Tis the middle watch of a summer night—
The earth is dark but the heavens are bright
The moon looks down on old Cronest,
She mellows the shades of his shaggy breast,
And seems his large grey form to throw
In a silver cone on the wave below.

This is almost as splendid a piece of versification as Mickle's famous

lines on Cumnor Hall by Sir Walter Scott in the preface to Kenilworth:

> The dews of summer night did fall,
> The moon sweet regent of the sky,
> Silvered the walls of Cumnor Hall
> And many an oak that grew thereby.

The Culprit Fay is full of much that is commonplace but there are some verses of exceptional beauty, worthy of a greater poet and showing a fine ear for both cadence and sound:

> The winds are whist and the owl is still
> The bat in the shelving rock is hid,
> And naught is heard on the lonely hill
> But the cricket's chirp and the answer shrill
> Of the gauze-winged katy-did.

The American Flag is a song that schoolboys of years ago were accustomed to see in their readers. The opening lines are familiar to many today as a poetical description of our flag:

> When Freedom from her mountain height
> Unfurled her standard to the air
> She tore the azure robe of night
> And set the stars of glory there.

Poe speaks somewhat slightingly of it and remarks that, "The deficiencies of the whole poem may be best estimated by reading it in connection with 'The Mariners of England,' or with 'Hohenlinden.' It is indebted for its high and most undeserved reputation to our patriotism and not to our judgment." However, the comparison is not so unfavorable as this assertion would make it appear as on putting it to the test suggested by Poe, the work of Dr. Drake does not suffer too much when contrasted with Campbell's more celebrated lines.

As much as by his own verse Drake will be remembered as having inspired one of the most beautiful elegies in English poetry. The Lines on the Death of Joseph Rodman Drake by his friend Halleck constitute a tribute of remarkable sincerity and beauty.

> Green be the turf above thee,
> Friend of my better days
> None knew thee but to love thee,
> Nor named thee but to praise.
>
> Tears fell when thou wert dying,
> From eyes unused to weep,
> And long, where thou are lying,
> Will tears the cold turf steep.
>
> When hearts whose truth was proven
> Like thine are laid in earth
> There should a wreath be woven
> To tell the world their worth.
>
> And I, who woke each morrow
> To clasp thy hand in mine,
> Who shared thy joy and sorrow,
> Whose weal and woe were thine.
>
> It should be mine to braid it
> Around thy faded brow,
> But I've in vain essayed it,
> And feel I cannot now.
>
> While memory bids me weep thee,
> Nor thoughts nor words are free,
> The grief is fixed too deeply,
> That mourns a man like thee.

All in all, we have in Drake a name of which every physician may well be proud. Though his medical activities were few he nevertheless reflected honor upon the profession as a man of letters and the charm of his personality is felt even today. A century after he is dead his sympathy, warmth, and friendliness leave a happy impression upon us.

# Editorial

## Some Physiological Effects of Golf

Karpovich in the American Physical Education Review for November, 1928, has reported the results of an investigation as to the physiological effects of golf, which should be of great interest to the many medical players of this game, not only to its possible effects upon themselves, but also with reference to its effects upon their patients. There are very few physicians, who, today, are not confronted with the question of advising patients either to play or not to play golf. When, as is usually the case, the patient is advised to play, unexpected sequelae not infrequently happen; and when they forbid the game the patient usually plays anyway, again with results that are often very different from those predicted. There is really nothing in the literature that is helpful in respect to the physiological or pathological effects of golf. Most of the literature as to the effects of golf is mere guess-work, written from the standpoint of enthusiastic rooters for the game, and concerned chiefly with its recreational aspects. In the very few books treating of golf from a medical standpoint, it has been chiefly from the point of view of the utilization of the game in the treatment of neurotic, or mentally abnormal individuals. But for the far greater number of normal individuals and those physically handicapped by organic lesions of heart, bloodvessels, kidneys, etc., there is no information available as to the advantages and disadvantages attendant upon golf playing. Golf has become extremely popular in this country during the last ten years, as is shown by the great increase in both private and municipal golf courses, and in the very large number of players. With all of its popularity opinions on the game differ widely. On the one hand we hear the game derided as fit only for old people and for the middle-aged who are beginning the descent of life. An "old ladies" game it has in the past been frequently called by the younger devotees of tennis and the more active sports. It is true that in any country club one sees a large proportion of men past the peak of life belonging to the tired business or professional man class; but on the other hand the game is rapidly being taken possession of by the younger generation, who claim that the real game of golf can be played only by youth. Striking proof of this contention is shown in the fact that the real golf champions belong to the younger set of players. On some links the older men are finding themselves in the way of aggressive youthful golfers. Golf is attracting the high school adolescent, and an increasing number of young people throng our links. And then there are tales of deaths of old people upon the links, from heart failure and apoplexy.

for which excessive physical exercise and too great excitement during the game are blamed. When one views the different groups of players, one is led to the view that both opinions are correct; on the one hand we have the player for whom golf is a recreation; on the other we have the record-breakers for whom the game is a continued effort. This investigation of Karpovich was stimulated by Dr. Frederick Brush, who is a medical director of the Burke Foundation for Convalescents, and is an expert golf player himself. Because of the uncertainty of the value of golf as a recreational and therapeutic method for the patients it was decided to start a research into the effect of golf upon the players. This was accomplished by an examination of 120 people; 90 of whom were thoroughly studied. Of these latter there were 16 men and 26 women golfers, 40 men and 8 women patients, 20 of these being cardiac cases. Most of the subjects played 18 holes on regular golf courses, some played 36. Usually it was a friendly game, sometimes a championship game. Weight, heart rate and blood pressure were taken in the reclining and standing positions.. Schneider's cardiovascular test was given before and after the game. Pulse pressure and product of it times the pulse rate (PP x PR) were used as possible checks of the changes in the organism of the player. Balance tests and examination of the urine were used in too few cases to be of value. The study resulted in making clear certain physiological facts, and suggested some clinical observations which are of interest and value to those who supervise exercise either with well or sick individuals. There was usually a decrease of weight after the game, ranging from one to four pounds. It was not a true loss because subjects were weighed in their clothes both times. Patients who did not show any change in weight drank plenty of water. In well individuals the heart rate rises with physical exercise, due to an increased metabolism. In general the heart returns to normal in a short while, often to subnormal for a short period. This study showed that the same thing was true for the well and convalescent cases. The rate of the heart beat and the time needed to return to the normal indicated the amount of energy expended. It was shown that women expend less energy in playing golf than do men. There was no indication that anyone overdid in the game. It is a well-established fact that the systolic blood pressure rises during exercise with a subsequent decline, and after cessation of work it drops to subnormal. This study showed a general drop in the reclining position and in the standing position, except in the patients who played on one of the courses laid out on a 4 per cent slope and not severely trapped. The diastolic pressure dropped in the reclining position generally for the women, and 48.6 per cent cases for the men with an increase in 43.9 per cent of cases. Cardiac patients on the same course showed an increase and 50 per cent a decreased pressure. There is much difference of opinion in regard to the significance of the rise or fall of the systolic pressure in the reclining and standing position after exercise. This

study threw no light upon this question. When the diastolic pressure was lower in the standing position than in the reclining position the examiner usually found some permanent or temporary lesion, such as intoxication, neurasthenia or heart disease. Schneider's index is an expressive index of condition, being greater in healthy people, and smaller in diseased people. People with heart disease or other lesions show a great fluctuation. People with thorough compensation show the least fluctuation. The test appears to be the best one to ascertain cardiovascular adjustment. It seems possible also to say that the greater the fall in the Schneider index the greater has been the demand upon the cardio-vascular system. From an increase in heart rate and a decrease in Schneider's index we may assume that the volume of circulation per minute is increased. The examiner found a decrease in pulse pressure after a game. The more exhaustive a game the greater was the decrease. It has been suggested that the pulse pressure times the pulse rate might serve as an index of the volume circulatory blood or circulation rate. On the basis of this study the PP x the PR may be used as a group index, but it did not bear out the idea that it is an exact index of the circulation rate. The study did suggest that if there is big drop in PP x PR that the blood circulation is inadequate. It is important to test the PP x PR in a standing and not in a reclining position immediately after the game. Based upon the study of individual cases it seems possible to draw the following conclusions: The great variability in Schneider's index in one and the same person may serve as an index of the variability of the cardiovascular conditions. A great drop in the usual pulse pressure in the standing position may indicate disturbance in circulation due to fatigue. If, in spite of an increase in the pulse rate in a standing position, there is a marked decrease in PP x PR, there is also indicated a disturbance in cardiovascular adjustment, which in most cases is coincident with well pronounced subjective feelings of fatigue, or of feeling "not well". Alcoholic intoxication and loss of sleep preceding the game causes a great drop in pulse pressure in a standing position after the game and lowers the endurance. In case of myocarditis there is very little change in all items after an easy game for half an hour on a small course. More prolonged games, and on longer courses, cause a marked drop in systolic blood pressure and pulse pressure, and usually the subject does not feel well. Three thousand yards of playing makes very little difference to a healthy man, when he plays with the same tempo all the time. Hearts with valvular lesions, but well compensated, react in the same way as sound hearts after a mild exertion. A strenuous game, as in tournaments, may cause a more rapid pulse on the next morning and a lower PP in the standing position. A mere friendly game has less effect on pulse rates and pulse pressure than a championship game. The heart rate increases and the PP decreases more in the latter case. In prescribing the game for patients, it is safe to begin with the half-hour game. The general

answer of the patient that he or she "feels fine" should never be taken as a criterion of the actual condition, but the real situation should be ascertained by other means. The following clinical observations were made on the strength of this study: A too great loss of weight following exercise with a slow return of weight is bad. Lower blood pressure particularly in the standing position with higher heart rate and a slow return to normal after very moderate exercise is an indication of poor condition. Sleeplessness, restlessness, fatigue in the morning and lessened appetite after moderate exercise is an indication of poor condition. Abnormal heart or kidney conditions increase the dangers in severe exercise. Moderate exercise cautiously taken will be of advantage. All individuals should be cautious about eating too soon after exercise. People out of condition should be very careful to rest before eating. Patients recovering after some sickness naturally have less endurance and may collapse even after playing a few holes. Usually they walk and play slowly, and it is better to allow them to play not more than thirty minutes on a plain, even course. There is strong evidence that such exercise is beneficial to them. If ill effects are seen, reduce the number of holes played. Cardiac patients with well developed compensation react in the same way as normal people, and 18 holes played by some do not seem to have any harmful eflect upon them. It would be of considerable interest to make actual measurements of the output of energy by golf players. There are no available figures expressing the amount of energy spent while playing golf. Yandell Henderson calls golf a vigorous game, Harrington says that the amount of work performed in going once over a course is very considerable. Using data found by F. Benedict we can attempt to give an approximate value of work done in going over a golf course with playing distance of 6000 yards, assuming that this course is on a perfect level. A person walking over this course at a speed of four miles an hour spends as much energy doing so as he would to lift himself five and a half times to the top of the Woolworth building, or walking with a speed of about two miles an hour he would spend enough energy to lift himself a little over four times to the top of the same building. As a matter of fact golf courses are usually located on hilly ground, and this greatly increases the output of energy necessary to cover the playing distance. To all of this we must add the work performed in practice and actual shots and in searching for the ball. It will be seen, therefore, that golf as it is usually played belongs to the more strenuous games, and the question of its advisability for the middle-aged and the old player is one not to be taken too lightly. In addition to the above resumé of Karpovich's study, the editor would add some practical observations of his own. In every country and golf club there are to be seen individuals actually in poor condition from the result of too much golf and of golf unwisely played, combined with other factors, too much food and alcohol. Who does not recognize the type—the florid, obese, or stout, gentleman of between

45 and 60 years of age—a successful business or professional man, who rides to and from his place of business every day, and who religiously plays golf once or twice weekly, thinking he is exercising to the good of his body, when in reality the manner and degree of this exercise is doing him positive harm. Before going upon the links he fortifies himself—the worst possible thing for him to do, in its effect upon his cardiovascular system—by a nip from his flask; and on coming in, red, perspiring, with a cyanotic hue to his floridness, with dilated cutaneous vessels, and increased heart rate—he, feeling more or less "all in", resorts to another nip, and then usually follows this with a beefsteak supper. This is the material from which the deaths on the links and in the club houses are recruited; golf when taken in this fashion predisposes to acute cardiac dilatation, coronary thrombosis and apoplexy. Golf is a fine game when played right—as a social, leisurely game, without strenuosity or the excitement of competition; when taken otherwise it becomes a very dangerous form of exercise to individuals of the successful, over-prosperous, arthritic type of build and constitution.

# Abstracts

*Diabetes Mellitus in the Negroes: A Study of One Hundred Consecutive Cases.* By Harold M. Bowcock (The Southern Medical Journal, December, 1928).

No comprehensive study of diabetes mellitus in the American negro has appeared in medical literature. This condition, as observed in the colored race, presents many interesting points of comparison and contrast with the same disease in the white race. The data from one hundred cases of diabetes mellitus occurring in the colored race have been subjected to statistical analysis. The disease occurs in pure blacks as well as mulattoes. The sex incidence in this series is predominantly female. In the large majority of cases the appearance of the disease has been preceded by marked obesity in the female patients. Syphilis has not seemed to be an important etiological agent. The disease is usually mild, and the greatest handicap to adequate control is poor cooperation due to poverty and lack of intelligence. The same complications appear in the negro and white diabetic. Successful results can be obtained in colored patients after paintaking instruction in the general principles of diet, insulin dosage and administration of insulin and the technic of testing urine for sugar. No metabolism experiments were performed upon these patients. Such studies will be made, because one is constantly impressed by the fact that the obese cases do not lose weight, even though they claim that they adhere to a diet yielding a very small caloric value; in some instances the food which the patient claims to be taking regularly could yield only 900 to 1,000 calories daily, as calculated from the diet lists submitted. Practically all of the clinic cases have been able to continue with, or to resume, their usual occupations. Thus the results obtained, although far from being ideal, when viewed from an economic standpoint justify the effort expended.

*An Experimental Study of Diathermy. VI. Conduction of High Frequency Currents Through the Living Cell.* By Ronald V. Christie (Jour. of Exper. Med., August, 1928, pp. 235-246).

In this paper an attempt has been made to correlate the investigation of biophysicists with those questions which are of fundamental importance in a study of diathermy. Biophysicists on the one hand have paid little attention to the phenomenon of heat production with the passage of high frequency currents, while those studying diathermy have neglected the problem of cellular correlation and penetration. It is obviously of great importance to know whether the diathermy current passes through the living cell and if so, what are the effects produced. The results of the experiments performed by Christie seem to show pretty conclusively that, with regard to its passage through biological media, the diathermy current behaves in the same manner as low voltage high frequency currents of the pure sine wave form. With both the laking of cells produces no change in impedance, and with both, an increase in cellular concentration of blood produces an impedance change which is characteristically lower than that found with low frequency currents. The cell membrane is a very efficient condenser which transmits the current by its capacitance with little or no dielectric loss, and consequently little or no stress and strain on the cell wall. Cellular massage is a term commonly met with in the literature of diathermy. There is no evidence to show that either this, or the electromechanical vibration which is said to occur with currents of a higher frequency, exists. Christie concludes that the diathermy penetrates the living cell, and heat production is intracellular as well as extracellular. A small proportion of the impedance of living cells as to the diathermy current seems not to lead to the production

of heat. Evidence is given that the addition of saponin produces an appreciable increase in the conductivity of an electrolyte. Its use is, therefore, contraindicated when electrical measurements are being made on biological material. The currents used in diathermy behave as do high frequency currents of the pure sine wave form in respect to their passage through biological material.

*Observations on Some Cardiac Lesions Coincident with Pulmonary Tuberculosis.* By I. D. Bronfin and Saling Simon (Amer. Rev. of Tuberculosis, December, 1928).

The coincidence of valvular heart disease and pulmonary tuberculosis is not as rare a condition as is generally supposed. Dyspnea out of proportion to the pulmonary involvement, especially when there are no constitutional symptoms, should arouse the suspicion of an existing cardiac affection. The absence of murmurs does not exclude the possibility of grave valvular affections. According to Broadbent a murmur is rarely heard in the third stage of mitral stenosis. It is of particular importance to the phthisiologist to remember that digestive disturbances, pressure pain in the epigastrium, gaseous eructations followed by temporary relief from the epigastric distress, paroxysmal attacks of dyspnea and cough, fatigue on the slightest exertion, disinclination or inability to concentrate on a physical or mental effort, and other well-known so-called neurotic symptoms, may be due as much to early cardiac decompensation as to active pulmonary tuberculosis. The proper evaluation of these symptoms is no small problem. The incidence of valvular heart disease in pulmonary tuberculosis, recognizable clinically, is only about 6 per cent in their experience. Artificial pneumothorax, when indicated in such cases, should be administered with great caution. The earliest manifestation of cardiac disturbance is an indication for discontinuing the pulmonary compression. Complete bed-rest must be rigidly enforced for a longer period of time than in cases not complicated by heart disease. The electrocardiogram is often of the greatest value in determining the course of obscure cardiac symptoms.

*The Preventorium Child. A Clinical Review of Three Hundred Cases.* By I. D. Bronfin (Amer. Jour. of Dis. of Children, November, 1928).

Clinical records of 300 preventorium children were reviewed, and a study made of the roentgenograms. An underweight of 7 per cent or more was found in 70 per cent. In 30 per cent fever was a prominent symptom. An appreciable difference was not observed in the symptomatology or physical signs between the tonsillectomized and the nontonsillectomized groups. The greatest incidence of clinical disease and positive physical signs was noted in those with a history of definite exposure. Physical signs were often negative when the history and symptoms pointed to active disease. The x-ray was of the greatest aid in diagnosis when correlated with the other symptoms. Of the entire series, only seventy-two roentgenograms of the chest were considered within the normal. Calcification at the hilum, strongly suggestive of tuberculosis, was observed in only 22 per cent, but it is believed that the incidence would have been greater if films in the oblique position had been taken. Primary foci were detected in 11.6 per cent and in 11.3 per cent there was noted a frank parenchymal pulmonary infilration. Attention is called to the difficulty of making a diagnosis of tracheobronchial tuberculosis, which in this series was frequently responsible for active symptoms and was often attributed to other causes. Under treatment symptomatic improvement invariably occurred. Unremitting supervision was necessary, for in many patients there was a recurrence of symptoms with increased physical activity. A notable recession was not noted in either the cervical or the tracheobronchial glands after prolonged periods of continued heliotherapy. Bronfin concludes that active juvenile tuberculosis is still unrecognized in the majority of instances; and that physical signs of juvenile tuberculosis are indefinite and often misleading. The history and symptoms are more important as a basis for treatment than are physical signs. The x-ray is of

the greatest aid in diagnosis. The practical solution of the problem of tuberculosis in adults depends in a large measure on the attention that is accorded children with latent or active tuberculosis. All patients who have been exposed to the disease should have a limited period of residence in a suitable hospital or should be under close medical supervision even in the absence of symptoms. Preventoriums for the observation of children who have been exposed and for the treatment of juvenile tuberculosis are needed as urgently as sanatoriums for the treatment of adults with tuberculosis.

*Hepatic Lesion in Eclampsia: An Experimental Study.* By William J. Dieckmann (Proc. of the Soc. f. Exper. Biol. and Med., December, 1928, p. 239).

The hepatic lesion in human eclampsia is peculiar in that it does not occur in any pregnant animal or in any other human disease. The lesion is essentially a thrombosis occurring in the capillaries of the portal vein in the periphery of the liver lobule with hemorrhage into the adjacent tissues, resulting in necrosis. Dieckmann believes that whatever the substance is which causes this thrombosis, it must be in greater concentration in the portal system. From clinical experience it is known that curtailment of protein together with intestinal elimination will in almost all cases prevent eclampsia. We also know that eclampsia does not occur unless the woman is pregnant, that is, living chorionic villi must be present. The fetus may be dead, for true eclampsia has occurred with hydatidiform mole. In late pregnancy placental fragments are constantly entering the blood stream. This placental tissue is rich in tissue fibrinogen, a blood coagulant found in tissue extracts, which must be neutralized or destroyed by substances in the blood. Mills has demonstrated that tissue fibrinogen, a cephalin-protein complex can pass through the intact intestinal wall and shorten the clotting time of the blood. If this is true it seems that the production of the hepatic lesion of eclampsia could be explained as follows: If too much of the neutralizing substance is used up by the placental tissue, it is conceivable that tissue fibrinogen from meat, by mouth, requiring the same detoxifying substance, could reach such a concentration in the portal system that thrombosis would occur. It was first necessary to see if portal thrombosis could be produced. Tissue fibrinogen prepared by the Merrel Drug Company according to Mills' directions was used, thus ruling out the possible effects of other substances which are found in tissue extracts. In order to get as great a concentration as possible in the portal system tissue fibrinogen was injected daily into the portal vein by use of the Blankenhorn cannula, at the same time injecting the substance in the peripheral circulation, thus simulating pregnancy. Doses of 2 to 5 ml. were used peripherally and 3 to 12 ml. for the portal. Eight dogs were treated in this manner, 3 of which showed lesions typical of eclampsia. The remainder all showed marked portal vein thrombosis and hemorrhage into the liver tissue, but only to some extent from the periphery of the lobule. The fact that marked thrombosis occurred was due to over dosing resulting in coagulation of the blood in the larger branches of the portal vein, which, therefore, interfered with the production of hemorhage. This work demonstrated that tissue fibrinogen used in this way in proper does could cause portal coagulation and produce a liver lesion similar to that of eclampsia. The present report is based on the combination of the peripheral injection and oral feeding of tissue fibrinogen. Seven dogs were fed fibrinogen in 3 ml. doses through a stomach tube and at the time there was injected 1 to 5 ml. peripherally. These experiments varied from 3 to 7 days in duration. In 7 cases, 3 showed liver hemorrhage in the gross, similar to that in eclampsia, 4 showed beautiful eclampsia lesions, and 5 showed portal vein thrombosis within the liver. One was entirely negative. The fact that limitation of protein prevents the development of eclampsia in many cases, and, furthermore, that a method of starvation and intestinal elimination gives the best results in curing the condition suggests strongly that substances which may be toxic to the pregnant woman

are absorbed from the intestinal tract. This report is primarily concerned with the hepatic lesion, but it may be noted briefly that some of the dogs had convulsions, tonic and clonic, and some became comatose. The development of these conditions depended on the dosage. Sections of the kidney in some animals showed lesions similar to those found in humans dying of eclampsia. The author believes that his findings explain in a measure why the hepatic lesion in eclampsia can be averted by limiting the protein intake of the patient in the last months of pregnancy.

*Clinical and Pathological Changes in Livers of Copper-fed Animals.* By William C. Von Glahn and Frederick B. Flinn (Proc. of the Soc. f. Exper. Biol. and Med., December, 1928, p. 200).

A study of the chemical and pathological effects of copper on the liver was made on a series of guinea pigs, albino rats and rabbits. Different groups of matured Belgian hares, kept on a standard diet of hay and oats, with cabbage and carrots on alternate days were fed daily doses of various copper salts. In each of the rabbits, yellow or yellowish brown refractile pigment was found in the liver cells. In some, pigment was also present in phagocytes in the portal areas and occasionally in connective tissue cells in the same region. In a few animals, some of the endothelial cells of the sinusoids contained pigment. Iron was not found in the pigment, which stained with fuchsin, but not with Sudan III, Scharlach R, nor with osmic acid. Nile blue sulphate colored the pigment greenish blue to deep blue. The amount of connective tissue in the portal areas varied in different portions of the same sections and in different animals, but was nowhere sufficiently developed to justify a diagnosis of cirrhosis. The amount of copper in the livers showed considerable variation even in the same group, though in general the livers of those animals receiving metallic copper had the largest amounts. Livers of rabbits dosed with sodium acetate contained pigment which had the same staining reaction as in the copper fed animals, the livers of normal rabbits contained pigment and identical variation in the quantity of connective tissue in the portal areas as were observed in copper fed rabbits. Rabbits fed carrots alone showed a marked increase in the quantity of pigment over that present in the piece of liver removed before the animals were kept exclusively on a carrot diet. Rabbits on a carrot diet did not show an increase in the pigment when fed copper over that observed in rabbits which were kept on carrots for only 14 days. Turnip-fed rabbits also showed a small amount of pigment. The results on guinea pigs and albino rats were entirely negative. From the above experiments it was concluded that copper does not cause pigmentation or cirrhosis of the livers of rabbits, rats or guinea pigs; and that the pigment found in the liver of rabbits is probably of exogenous origin.

# Reviews

*The Mechanics of the Digestive Tract. An Introduction to Gastroenterology.* By WALTER C. ALVAREZ, M.D., Associate Professor of Medicine, University of Minnesota (The Mayo Foundation). Second Edition. 447 pages, 100 illustrations. Paul B. Hoeber, Inc., New York, 1928. Price in cloth, $7.50

The first edition of this work was published five years ago. It was little more than a detailed statement of the gradient theory of activity down the intestine with its bearings on the problems of gastroenterology. This new edition has been entirely rewritten, and represents a determined effort to make readily available to practitioners such information about the mechanics of the digestive tract as they need daily in their attempt to improve their diagnostic and therapeutic technic. During the five years between the two editions the gradient theory has received considerable support from various workers and a number of the author's early observations have been confirmed. The experimental studies of Pavlow, Baylis, Starling, Cannon, Carlson, Ivy and others are put together with his own original observations to give the clinician a practical point of view. The present knowledge of the process of digestion is summarized and the experimental and clinical work upon which this knowledge rests are described in detail. Alvarez' original gradient theory of the gastrointestinal tract is naturally explained in detail and constitutes the chief motive of the book. A thorough review of our knowledge of peristalsis both in health and in disease is included. The table of contents includes: The Autonomy of the Digestive Tract; the Myogenic Nature of the Rhythmic Contractions; the Function of Auerbach's Plexus; the Smooth Muscle of the Gastrointestinal Tract; the Extrinsic Nerves and Their Functions; Why Food Goes Down the Bowel; Gradients; Underlying Metabolic Gradient; Other Related Gradients; Chewing and Swallowing; the Esophagus; Cardia; Graded Differences in the Stomach Wall; Movements of the Stomach; Hunger Contractions and the Pain of Ulcer; The Movements of the Stomach that is Diseased or Has Been Operated Upon; Modus Operandi of a Gastroenterostomy; Pylorus and Pyloric Cap; Movements of the Small Intestine; Ileocecal Sphincter; Movements of the Colon; Mechanics of the Gallbladder; Rate of Progress of Food Residues through the Digestive Tract; Vomiting; Practical Applications of the Gradient Idea; Reverse Peristalsis and Its Symptoms; Flatulence and Technical Methods and Apparatus. By gradient Alvarez means a gradation in some attribute, a state, force or activity which is to be found between certain limits in space or time. It is an expression of relationship; There are probably a number of gradients, all related, all serving to direct peristalsis caudad, and all based on some fundamental gradation in the structure or in the metabolic rate of the contractile tissues. Waves tend to spread out in both directions from a stimulated place in a muscular tube; a gradation in rhythmicity makes it easier for the waves to go in one direction than in the other, thus in the bowel caudad rather than cephalad. The basis gradient in an organ must be fundamental and not the result of functional adaptation. Most of the symptoms of gastrointestinal disease are due to disturbances in the mechanical functions. The book is an interesting exposition of the gradient theory of the gastrointestinal musculature, and throws new light upon many gastrointestinal disturbances. From it the clinician can obtain new viewpoints of much practical value. The book is highly recommended to physicians, sur-

geons and radiologists. For the researcher engaged in this line the very full bibliography is an important and valuable feature of the book. The illustrations are satisfactory, and the printing excellent.

*William Harvey.* By ARCHIBALD MALLOCH, M. D., (McGill), M. R. C. P. (Lond.), Librarian, N. Y. Academy of Medicine. 103 pages, 10 full page plates and 3 text illustrations. Paul B. Hoeber, Inc., New York, 1929. Price $1.50.

This delightful little account of Harvey's life by Malloch is reprinted, with corrections, from The American Journal of Surgery (New Series, Vol. V, Nos. 3 and 4, September and October, 1928.). It originated as a tercentenary address delivered at a joint meeting of the Harvard Medical Society and the Boston Medical History Club held on the twenty-fourth of April at the Peter Bent Brigham Hospital. It is hoped that medical students, doctors and others will welcome a sketch of the life and work of one of the greatest scientists and physicians, and that they will be stimulated towards further reading of these fascinating subjects, the history of science and the biography of its great men. An attempt has been made in this sketch to show how a knowledge of the circulation was painfully and slowly won in the centuries before Harvey and exactly how the latter arrived at the important conclusion that the blood moved in a circle. In this Malloch has been particularly successful. The contents of the chapters are given to a consideration of the following: Harvey's education, a day with Harvey, publication of the book on the circulation, Harvey's predecessors, the movement of the heart, the circulation, further proofs, tour on the continent and return to London, the witches, another continental tour, civil war, Oxford, London, the book on generation, Harvey and the College of Physicians, his death, burial and will. The illustrations comprise the title page of the first edition of "De Motu Cordis", Harvey's Stemma at Padua, the anatomical theatre of Fabricius at Padua, Harvey's pointer or wand, Harvey demonstrating to Charles I his discovery of the circulation of the blood, Edward's engraving of William Harvey, Harvey's letter to Lord Dorchester, Title Page of first edition of "De Circulatione Sanguinis", Frontispiece of first edition of "De Generatione", engraved title page of Elzevir edition of "De Generatione" with London imprint, portraits of William Harvey and Hempstead Church. The story of Harvey's life is concisely told by Malloch in a pleasant conversational manner. One gets from it a very living impression of Harvey's times, education, method of delivering lectures and the ordinary routine of a day in Harvey's life. The speculations concerning the printing of the book on the circulation, as to why it was printed and published in Frankfurt and by Wilhelm Fitzer who never published any other important medical or scientific book, are just sufficiently touched upon as to excite the reader's interest in the problems of the first publication of the great book. The chapter on Harvey's predecessors is a well-accomplished bit of condensation of an enormous mass of available material and those on the movement of the heart, the circulation and further proofs, give the essence of Harvey's great discovery, told in an original and pleasant manner. The story of Harvey's connection with Lancashire witches shows his independence of minds and freedom from the superstition of the times. This is a pocket book that every practitioner should own and carry about with him until he has made the story of the great discovery and the great discoverer his own intellectual property.

*Laboratory Diagnosis and Experimental Methods in Tuberculosis.* By HENRY STUART WILLIS, The Johns Hopkins University and Hospital. With a Chapter on Tuberculo-Complement Fixation, by J. Stanley Woolley, Loomis Sanatorium, Loomis, New York. Introduction by Allen K. Krause, The Johns Hopkins University. 333 pages, 25 illustrations. Charles C. Thomas, Springfield, Illinois-Baltimore, Maryland, 1928. Cloth: $3.50; Keratol: $4.25.

This book has a twofold purpose. It aims to describe the more important methods of the laboratory diagnosis of tuberculosis and

to consider some of the more significant procedures and principles involved in the experimental study of the infection. In the first instance it has brought together into one chapter a consideration of the fluids, secretions and excretions of the tuberculous body. Following this, it enters into an exposition of methods for the detection of the tubercle bacillus by staining, isolation and animal inoculation, and gives a description of this microörganism and compares it with other acid-fast bacteria, and deals with serological diagnosis and with diagnosis by the use of tuberculin. Secondly it devotes a number of chapters to some of the general factors concerned in the infection of animals and the study of experimental tuberculosis. The guiding principle of the author, as expressed in the preface, has been to cover the subject as concisely as is consistent with adequacy of presentation. Therefore, he has sought to present clearly in each of the various parts of the book only so many of the available technical procedures as appeared to him to be commensurate with the immediate subject at hand, always with an eye to the conservation of space and the prevention of too much duplication of essentially similar methods. Of the methods outlined, most have proved dependable through long application, but a few have been included which are new and virtually untried, because selection has occasionally been made on promise and rationale as well as on demonstrated worth. This plan has led to the omission of many methods, some of them of unquestioned value. It was the author's desire to write a book which would be useful to practising physicians, to public health officials and laboratory workers in general and to medical students. Part I deals with the General Consideration of the Body Fluids and Excreta in Tuberculosis; Part II treats of Bacteriologic Diagnosis, with Chapters on the demonstration of the tubercle bacillus by staining methods, by methods of concentration and isolation, and by the inoculation of animals, and a discussion of the tubercle bacillus, its cultivation, and the non-pathogenic acid-fast bacteria; Part III treats of Diagnosis by Use of Tuberculin, with Chapters on tuberculin and its preparation, and the diagnostic application of tuberculin; Part IV treats of Serological Diagnosis with Chapters on the Tuberculo-Complement Fixation and other Serological tests; Part V treats of Methods of Value in Studies of Tuberculosis Experimentally Produced, with Chapters on the inoculation of animals with the tubercle bacillus, induced tuberculosis in animals, methods of studying induced tuberculosis in animals, and histologic technique, while the final chapter treats of the equipment for a tuberculosis laboratory, with bibliography and index. The author has performed a most useful service in bringing together the various laboratory procedures that are concerned with the diagnosis and treatment of tuberculosis, as well as those adapted to research work in tuberculosis. It appears on inspection to have achieved most acceptably the aim set forth in the author's preface. A good word may be said for the new publishing house of Charles C. Thomas in the general excellence of this production, both as to printing and binding. It is a very neat job.

*The Pressure Pulses in the Cardiovascular System. Monograph on Physiology.* By CARL J. WIGGERS, M. D., Professor of Physiology in the School of Medicine of Western Reserve University, Cleveland, Ohio. 200 pages, with diagrams and illustrations. Longmans, Green and Co., London-New York-Toronto, 1928. Price: $5.00

The book is dedicated to Graham Lusk. Its object has been the analysis, in the briefest manner possible, of the present status of our knowledge concerning the pressure pulses in the cardiovascular system. Apparatus for making cardiodynamic studies, comparable in accuracy to physical instruments used for other types of physiological investigation has been available for a comparatively short time only. Its use under controlled experimental conditions demands a specialized technique, and the evaluation of records must be tempered by an insight gained only by years of service. Consequently this important method for investi-

gating the dynamics of the heart and circulation has not been extensively employed. It may be safely asserted that the number of investigators can be counted on the digits of two hands. It is, therefore, the author's hope that aside from its use as a reference medium and its value as a review of the subject, this little book may encourage others to enter this fascinating and precise field of investigation. Chapter I is concerned with the evolution of graphic methods for registering pressure pulses; Chapter II with the registration of pressure curves by micro-manometers; Chapter III with the configuration of pressure pulses in the cavities of the heart; Chapter IV with sequence of cardiodynamic events as established by pressure pulses from the auricles, ventricles and the aortae; Chapter V with the arterial pulse; Chapter VI with the venous pulse; Chapter VII with the consecutive phases of the cardiac cycle and the criteria for this precise determination; Chapter VIII and IX with the response of the heart to physiological variable; Chapter X with the intimate character of the ventricular contraction and Chapter XI with the pressure pulses under certain abnormal types of ventricular contraction. There follows a bibliography and an index. This little volume succeeds admirably in the presentation of the facts concerning the pressure pulses and in the evaluation of the experimental results. The book is an important addition to the Monographs on Physiology edited for so many years by the late Ernest Starling. In that series he stated that it was intended to set out the progress of physiology in those chapters in which the forward movement was the most pronounced. Dr. Wiggers' book has been most successful in accomplishing this intent and purpose, in so far as the knowledge of the pressure pulses is concerned. The illustrations are numerous and to the point. The very complete bibliography is of great value; twenty-seven of the papers included are by Wiggers himself, good evidence of his ability to deal authoritatively with the subject.

*Studies on Scurvy. Stanford University Publications, Medical Sciences, Volume II, Number* 2. By ARTHUR W. MEYER AND LEWIS M. MCCORMICK. 108 pages, numerous illustrations. Stanford University Press, Stanford University, California, 1928. Price: paper $1.50; cloth $2.50.

*The Symptomatology and Gross Morphology of Experimental Scurvy in the Guinea Pig, by* ARTHUR W. MEYER; *the Minute Morphology of Experimental Scurvy in the Guinea Pig,* by ARTHUR W. MEYER; and *Some Characteristics of the Blood of the Guinea Pig in Experimental Scurvy,* by LEWIS M. MCCORMICK.

This monograph consists of three parts. The Symptomatology and Gross Morphology of Experimental Scurvy in the Guinea Pig, by Arthur W. Meyer; the Minute Morphology of Experimental Scurvy in the Guinea Pig, by Arthur W. Meyer; and Some Characteristics of the Blood of the Guinea Pig in Experimental Scurvy, by Lewis M. McCormick.

A so-called synthetic, basic diet was not used in these experiments because the original object was to ascertain, if possible, the causes for the appearance of peculiar phenomena in guinea pigs kept on ordinary feeds and used in experimental anatomy. Among these phenomena were marked nervous manifestations and permanent, as well as temporary, locomotor disabilities. Regarding these symptoms as indicating scurvy, the new observations upon the gross pathology of experimental scurvy as reported by Meyer are: The highly nervous condition of some of the animals; the recovery of health of young pigs after a condition of complete helplessness in the posterior half of the body; the occurrence of permanent locomotor disabilities; shortening of the roots of the teeth by absorption so that the molars can be depressed below the level of the gums; the occurrence of pronounced gaseous distention of the stomach in some animals and pseudopneumonic lesions in the lungs of others; fatty change in the liver, adrenals and other organs; necrotic areas in both liver and adrenals; and degenerative changes in and fibrosis of the costal cartilages even in regions remote from the costochondral

junctions. Some subcutaneous and muscular hemorrhage was almost always present, while duodenal, cecal, vesical and paravesical hemorrhages were common. The minute morphology showed hemorrhages in all parts of the body except in the gums and joints. There was a marked fatty infiltration and degeneration of the liver, kidneys, adrenals, and even in the lungs and the peribronchial cartilages, the pancreas, skeletal muscles and the blood walls. Degenerative changes other than fatty, resulting in the complete loss of substance, were observed in the cartilages, bones, teeth, muscles, many of the glandular organs, as well as in the central, peripheral and sympathetic nervous systems. This widely distributed liquefaction of the cytoplasm and cell walls results in destruction of cartilage cells and of the cartilaginous matrix, at least in the costal cartilages; in the detachment of the periostea and peridontia; in reduction in caliber of the bones, and in both the caliber and the length of the implanted portions of the teeth. It may effect not only the separation of ununited epiphyses and loosening of the teeth but the complete destruction of the parenchyma of some areas in the glandular and other organs, in desquamation of the mucosa and renal epithelium, and in complete disintegration of the walls of blood vessels. In addition to the fatty and lytic changes, coagulative changes, such as extreme waxy degeneration in the muscles, were also noted in glandular and nervous tissues. The only proliferative changes noted occurred in the costal cartilages and concerned an increase in caliber at the region of the costochondral junctions and an invasion of connective tissue into areas of degeneration. Necrotic areas on the surface and in the substance of the liver were occasionally observed, but may be wholly unrelated to scurvy. Vacuolation was common to many organs, and fenestration up to a marked degree was observed, especially in muscle, bone marrow, the pulp of the teeth, and also in the cord and brain. Definite cytological changes occurred in the blood of guinea pigs in experimental scurvy. These changes became evident after ten days on the scorbutic diet. They consist of a decrease in red cells, hemoglobin and color index, and apparent decrease in fragility, a relative decrease in the number of lymphocytes, an absolute increase in the polymorphonuclears, and an increase in reticulated and nucleated red blood cells and leukocytes. The eosinophile, basophile, monocyte and transitional cell counts were not considered characteristic of scurvy.

# College News Notes

# PROGRAM
## THIRTEENTH ANNUAL CLINICAL SESSION

### BOSTON COMMITTEES

JAMES H. MEANS, *General Chairman*

### COMMITTEE ON ARRANGEMENTS

JAMES H. MEANS
WILLIAM B. BREED
HENRY A. CHRISTIAN
RANDALL CLIFFORD
CHESTER M. JONES
ELLIOTT P. JOSLIN
ROGER I. LEE
GEORGE R. MINOT
JOHN H. MUSSER
JOHN PHILLIPS
JOSEPH H. PRATT
FRITZ B. TALBOT
CONRAD WESSELHOEFT
FRANKLIN W. WHITE

### COMMITTEE ON HALL

FRANKLIN W. WHITE

### COMMITTEE ON CLINICS

HENRY A. CHRISTIAN
CHESTER M. JONES
ELLIOTT P. JOSLIN
GEORGE R. MINOT
JOSEPH H. PRATT
CONRAD WESSELHOEFT

### COMMITTEE ON ENTERTAINMENT

RANDALL CLIFFORD
WILLIAM B. BREED
FRITZ B. TALBOT

### PRELIMINARY PROGRAM
### ANNUAL CLINICAL SESSION
### THE AMERICAN COLLEGE OF PHYSICIANS
### APRIL 8-12, 1929

Monday, April 8, 1929

OPENING SESSION, 2:30 O'CLOCK

Hotel Statler Ballroom

1. Addresses of Welcome. David L. Edsall, Dean of Harvard Medical School. Alexander S. Begg, Dean of Boston University Medical School. A. Warren Stearns, Dean of Tufts College Medical School. John M. Birnie, President of Massachusetts Medical Society. Lincoln Davis, President of Suffolk District Medical Society.

2. Reply to Addresses of Welcome. Charles F. Martin, President of The American College of Physicians.

3. Tuberculosis: A Confession of Faith. Lawrason Brown, Saranac Lake, N. Y.

4. (Title not yet announced.) Lewellys F. Barker, Baltimore.

5. Juvenile Diabetes. I. M. Rabinowitch, Montreal.

6. Glycosuria. James E. Paullin, Atlanta.

7. Clinical Aspects of Paroxysmal Hypertension. M. C. Pincoffs, Baltimore.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

*Symposium on Deficiency Diseases*

1. The Fundamental Nature of Deficiencies. George R. Minot, Boston.

2. Pathology of Deficiencies. S. Burt Wolbach, Boston.

3. Biochemistry and Physiology of Deficiencies. George R. Cowgill, New Haven.

4. Pernicious Anemia. Randolph West, New York.

Tuesday, April 9, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 TO 5:00 O'CLOCK
Hotel Statler Ballroom

1. Fatigue and Infection. W. L. Holman, Toronto.

2. Neoplasms. J. B. Murphy, New York.

3. Specific Dynamic Action of Protein, Fat and Carbohydrate in Altered States of Nutrition. Edward H. Mason, Montreal.

4. The Relation of Neisserian Infection to the Various Types of Arthritis. O. H. Perry Pepper, Philadelphia.

5. The Fallacy of Vaccine Therapy. Charles C. Bass, New Orleans.

6. The Treatment of Angina Pectoris. Harlow Brooks, New York.

7. The Coronary Problem. Arthur R. Elliott, Chicago.

8. Clinical Aspects of Trichiniasis. Lewis A. Conner, New York.

9. An Intensive Clinical Study of a Graphic Method of Recording Blood Pressure. Louis F. Bishop and Louis F. Bishop, Jr., New York.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

1. Psychiatry in Relation to Medicine. Austin F. Riggs, Stockbridge, Mass.

2. Syphilis of the Adrenals and Its Relationship to the So-called Idiopathic Addison's Disease. Aldred S. Warthin, Ann Arbor.

3. Lung Syphilis. R. I. Rizer, Minneapolis.

A *smoker* will follow this session.

Wednesday, April 10, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. The Treatment of General Paresis. Harry C. Solomon, Boston.

2. Psychiatry's Part in Preventive Medicine. Arthur H. Ruggles, Providence.

3. The Need of Emotional Data in the Medical History. John Favill, Chicago.

4. Milder Forms of Coronary Obstruction. James B. Herrick, Chicago.

5. The Failing Heart of Middle Life. David Riesman, Philadelphia.

6. Hypertension. George C. Hale, London, Ont.

7. Undulant Fever in the United States. George Blumer, New Haven.

8. (Title not yet announced.) Robert A. Cooke, New York.

9. Tobacco Smoking and Gastric Symptoms. Irving Gray, Brooklyn.

EVENING SESSION, 8:00 O'CLOCK
Hotel Statler Ballroom

1. Serums and Vaccines in the Prevention and Treatment of Disease. Benjamin White, Boston.

2. Clinico-Roentgenological Conference. M. C. Sosman and Associates, Boston.

Thursday, April 11, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. The Treatment of Acute Asphyxia. Cecil K. Drinker, Boston.

2. The Significance of Abnormal Metabolic Features in the Management of Thyrotoxicosis. Walter W. Palmer, New York.

3. Can or Will the Internist Practice Preventive Medicine? George H. Bigelow, Boston.

4. Factors in the Prognosis of High Blood Pressure. W. W. Herrick, New York.

5. The Carotid Sinus Reflex (Hering); Its Use in the Diagnosis and Treatment of Certain Cardiovascular Diseases. C. Saul Danzer, Brooklyn.

6. Lead Poisoning from Snuff. Raymond J. Reitzel, Galveston.

The General Business Meeting of The College will be held at 4:00 in the Hotel Statler Ballroom. All Masters and Fellows should attend.

EVENING, 7:00 O'CLOCK

Annual Banquet of The College
To be followed by a Dance.

Address: George E. Vincent, President of Rockefeller Foundation.

Friday, April 12, 1929
MORNING, 9:00 TO 12:00 O'CLOCK
Hospital Clinics

AFTERNOON, 2:30 O'CLOCK
Hotel Statler Ballroom

1. Motion Picture: Demonstrating Its Value in Teaching Electrocardiographic Interpretations of Cardiac Arrythmias. Joseph B. Wolffe, Philadelphia.

2. Dr. William Dunlop and Pioneer Canadian Medicine. J. W. Crane, London, Ont.

3. Rheumatic Fever. Homer F. Swift, New York.

4. (Title not yet announced.) J. C. Meakins, Montreal.

5. Results to Be Expected in Malignant Disease Treated by Radiotherapy. George E. Pfahler, Philadelphia.

6. The Problem of the Nervous Patient. Charles H. Nielson, St. Louis.

7. Endogenous Obesity—A Misconception. L. H. Newburgh and M. W. Johnston, Ann Arbor.

EVENING SESSION, 8:00 O'CLOCK

Hotel Statler Ballroom

Convocation Exercises

The General Profession is cordially invited. No special admission tickets are required.

1. Convocation Ceremony.

2. President's Address. Charles F. Martin, Montreal.

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## PRELIMINARY PROGRAM OF SPECIAL CLINICS AND DEMONSTRATIONS

This year the general session will be held in the afternoons and evenings, while clinics and demonstrations will be held in the mornings from 9:00 to 12:00.

Special Admission Cards required. Clinic reservation forms and full directions will accompany the Final Program. Reservations may be made by mail or daily at the Registration Bureau.

Special clinics and demonstrations will be held as follows:

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A

### BETH ISRAEL HOSPITAL

Program in charge of Herrman L. Blumgart

B

## BOSTON CITY HOSPITAL

1. (A guest will give a clinic at this time; the name will be announced later.)

2. The Progress of the Boston City Hospital. John J. Dowling, Superintendent.

3. Treatment of Pneumonia. Demonstration of Cases. Edwin A. Locke.

4. Clinic of Unusual Cases. Francis W. Palfrey.

5. Pernicious Anemia. Demonstration of Cases. William B. Castle.

6. Treatment of Anemias. Demonstration of Cases. George R. Minot.

WEDNESDAY, APRIL 10, 1929

1. (A guest will give a clinic at this time; the name will be announced later.)

2. Gastro-Intestinal Cases. Franklin W. White.

3. Cardiac Cases. William H. Robey.

4. Nephritis Cases. William R. Ohler.

5. The Surgical Treatment of Pulmonary Tuberculosis. Demonstration of Cases. Edward D. Churchill.

Hypertension and Arteriosclerosis. Demonstration of Cases. Soma Weiss.

THURSDAY, APRIL 11, 1929

1. Cardiac Cases. Edward N. Libby and Thomas J. O'Brien.

2. A Case Illustrating the Value of the Electrocardiogram. James M. Faulkner.

3. Epilepsy. William G. Lennox.

4. Diseases of the Coronary Vessels. Demonstration of Cases. Joseph T. Wearn.

5. Peptic Ulcer. Demonstration of Cases. Maurice Fremont-Smith.

6. Neurological Cases. Stanley Cobb.

7. (A guest will give a clinic at this time; the name will be announced later.)

FRIDAY, APRIL 12, 1929

1. (A guest will give a clinic at this time; the name will be announced later.)

2. Cases of Disease of the Hemopoietic System. Ralph C. Larrabee.

3. Lymphoblastoma. Demonstration of Cases. Henry Jackson, Jr.

4. Tropical Diseases. Demonstration of Cases. George C. Shattuck.

5. Fluoroscopic Diagnosis in Chest Conditions. Demonstration of Cases. Harold W. Dana.

6. Carcinoma of the Head of the Pancreas. Demonstration of Cases. Irving J. Walker.

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C

## BOSTON CITY HOSPITAL
## THORNDIKE MEMORIAL LABORATORY

WEDNESDAY AND THURSDAY

APRIL 10 AND 11

BETWEEN 10:30 AND 12:30

Demonstration of Researches Concerning the Following Topics

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| Dr. Castle and Associates | Anemia |
| Dr. Jackson and Associates | Malignant Tumors |
| Dr. Lawrence and Associates | The Physiology and Pathology of White Cells |
| Dr. Lennox | Epilepsy |
| Dr. Minot and Associates | The Blood |
| Dr. Nye and Associates | Bacteriological Problems |
| Dr. Wearn and Associates | The Capillaries |
| Dr. Weiss and Associates | Vascular Problems |

## BOSTON CITY HOSPITAL
## SOUTH DEPARTMENT

Program in charge of Edwin H. Place

Ward visits on (1) diphtheria, (2) scarlet fever, (3) a few of the other minor groups such as chicken pox, mumps, measles and whooping cough.

Amphitheater demonstration of cases of chronic laryngeal injury and other damages resulting from contagious diseases.

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## BOSTON DISPENSARY

TUESDAY, APRIL 9, 1929

1. Heart Disease. David Davis.
2. Essential Hypertonia. David Ayman.
3. Neurological Clinic. A. Warren Stearns.
4. Obesity. Mark Falcon-Lesses.
5. Gastro-Intestinal Clinic. Percy B. Davidson.

WEDNESDAY, APRIL 10, 1929

1. Bronchiectasis. William Dameshek.
2. Psychalgia. Joseph H. Pratt.
3. Arthritis. John D. Adams.
4. Chronic Pancreatic Disease. Bert B. Hershenson.
5. Tuberculosis. H. Louis Kramer.

THURSDAY, APRIL 11, 1929

1. Neurosyphilis. Arthur Beck.
2. Neurasthenia. Joseph H. Kaplan.
3. Nephrosis. Tobert W. Buck.
4. Domiciliary Medicine in Clinical Teaching—Selected Case. Osadore Olef.
5. Domiciliary Medicine in Clinical Teaching—Selected Case. Charles Korb.
6. Diabetes. James H. Townsend.

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F

## CHILDREN'S HOSPITAL

Program in charge of Kenneth D. Blackfan

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G

## HOMEOPATHIC HOSPITAL
## EVANS MEMORIAL CLINIC

TUESDAY, APRIL 9, 1929

1. Sterility Clinic. Special Emphasis to be Placed on the Constitutional Factors in Sterility. S. R. Meaker and A. W. Rowe.

WEDNESDAY, APRIL 10, 1929

*Endocrine Clinic*

1. Endocrine Diagnosis and Therapy. Charles H. Lawrence.
2. Endocrine Disorders Associated with Otosclerosis and the Menière Syndrome. D. W. Drury.
3. Eye Findings in Endocrine Disorders. W. D. Rowland.
4. Cases Presenting Outward Evidence of Endocrine Disorders Found on Study not to have Endocrine Disturbance. A. W. Rowe.
5. Dementia Praecox. L. G. Hoskins.
6. The Follicular Hormone. J. C. Janney.
7. Discussion on Sugar Metabolism as Influenced by Insulin in Pituitary Disease. H. Ulrich and A. W. Rowe.

THURSDAY, APRIL 11, 1929

*General Medical Clinic*

1. Heart Clinic. W. D. Reid.
2. Intestinal Migraine. C. W. McClure.
3. Neurology. N. H. Garrick.
4. Lung Abscess, Diagnosis and Treatment: Bronchoscopy, the Use of the Bronchoscope in Diagnosis and Treatment. L. R. Johnson.

FRIDAY, APRIL 12, 1929

(Program to be announced later.)

## H MASSACHUSETTS GENERAL HOSPITAL

1. Clinic by James E. Paullin, Atlanta.
2. Thoracic Clinic. Frederick T. Lord.
3. Cases of Hypertension. William B. Breed.
4. Cardiac Clinic. Howard B. Sprague.
5. Endocrine Clinic. Walter Bauer and Dwight L. Sisco.

WEDNESDAY, APRIL 10, 1929

1. Clinic by Lewellys F. Barker, Baltimore.
2. Demonstration of Medical Cases. William B. Robbins.
3. Pediatric Clinic. Fritz B. Talbot and Harold L. Higgins.
4. Clinico-pathological conference. Richard C. Cabot and Tracy B. Mallory.
5. Diabetic Clinic. Roy R. Wheeler.

THURSDAY, APRIL 11, 1929

1. Clinic by O. H. Perry Pepper, Philadelphia.
2. Neurological Clinic. James B. Ayer.
3. Psychotherapy of Gastro-Intestinal Diseases. William Herman.
4. Gastro-Intestinal Clinic. Chester M. Jones.
5. Indications for Splenectomy. Arlie V. Bock.
6. Cases of Pernicious Anemia. Wyman Richardson.

FRIDAY, APRIL 12, 1929

1. Clinic by J. C. Meakins, Montreal.
2. Demonstration of Cases. Gerald Blake.
3. Medical Clinic. James H. Means.
4. Demonstration of Cases. F. Dennette Adams.
5. Anaphylaxis Clinic. Francis M. Rackemann.

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## I NEW ENGLAND BAPTIST HOSPITAL

Program in charge of Albert A. Hornor

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## J NEW ENGLAND DEACONESS HOSPITAL

Program in charge of Elliott P. Joslin

1. Carcinoma of the Colon and Colitis from the Surgical Point of View. Daniel F. Jones.
2. Gastro-Intestinal Cases. Sara M. Jordan and Chester Kiefer.
3. Thyroid Cases. Frank H. Lahey.
4. Pedigreed Diabetics. Elliott P. Joslin.
5. Surgery in Diabetics. L. S. McKittrick.
6. The Pathology of Diabetes. Shields Warren.

There will be further additions to this program including clinics by larynologists, ophthalmologists, gynecologists and roentgenologists.

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## K PETER BENT BRIGHAM HOSPITAL

1. Diagnosis of Certain Forms of Heart Disease. Lewis A. Conner, New York.
2. Chronic Myocardial Disease. Henry A. Christian.
3. Results of Treatment of Duodenal Ulcer. E. S. Emery.
4. Some Considerations on the Relation of Cardio-Renal System to Surgery of the Urinary Organs. William S. Quinby.
5. Bronchoscopy in Lung Disease. Lyman C. Richards.

WEDNESDAY, APRIL 10, 1929

1. Cardiac Disease, the Result of Infectious Processes. James B. Herrick, Chicago.

2. Gallbladder Disease. Channing Frothingham.

3. Bronchial Asthma. I. Chandler Walker.

4. Anemia. William P. Murphy.

5. Thrombophlebitis. John Homans.

THURSDAY, APRIL 11, 1929

1. Mitral Stenosis. David Riesman, Philadelphia.

2. Signs of Persisting Infection in Acute Rheumatic Fever. Clifford L. Derick.

3. Hemorrhagic Nephritis. James P. O'Hare.

4. A Surgeon's Views of the Treatment of Peptic Ulcer. David Cheever.

5. Neurosurgical Conditions. Harvey Cushing.

FRIDAY, APRIL 12, 1929

1. Hypertension. Charles F. Martin, Montreal.

2. Vascular Disease in Diabetes Mellitus. Reginald Fitz.

3. Treatment of Certain Types of Cardiac Arrhythmia. Samuel A. Levine.

4. Treatment of Trifacial Neuralgia. Gilbert Horrax.

5. Diuretics. Henry A. Christian.

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L

## ROBERT BRECK BRIGHAM HOSPITAL

Program in charge of Louis M. Spears
Clinics on Arthritis

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M

## UNITED STATES NAVAL HOSPITAL

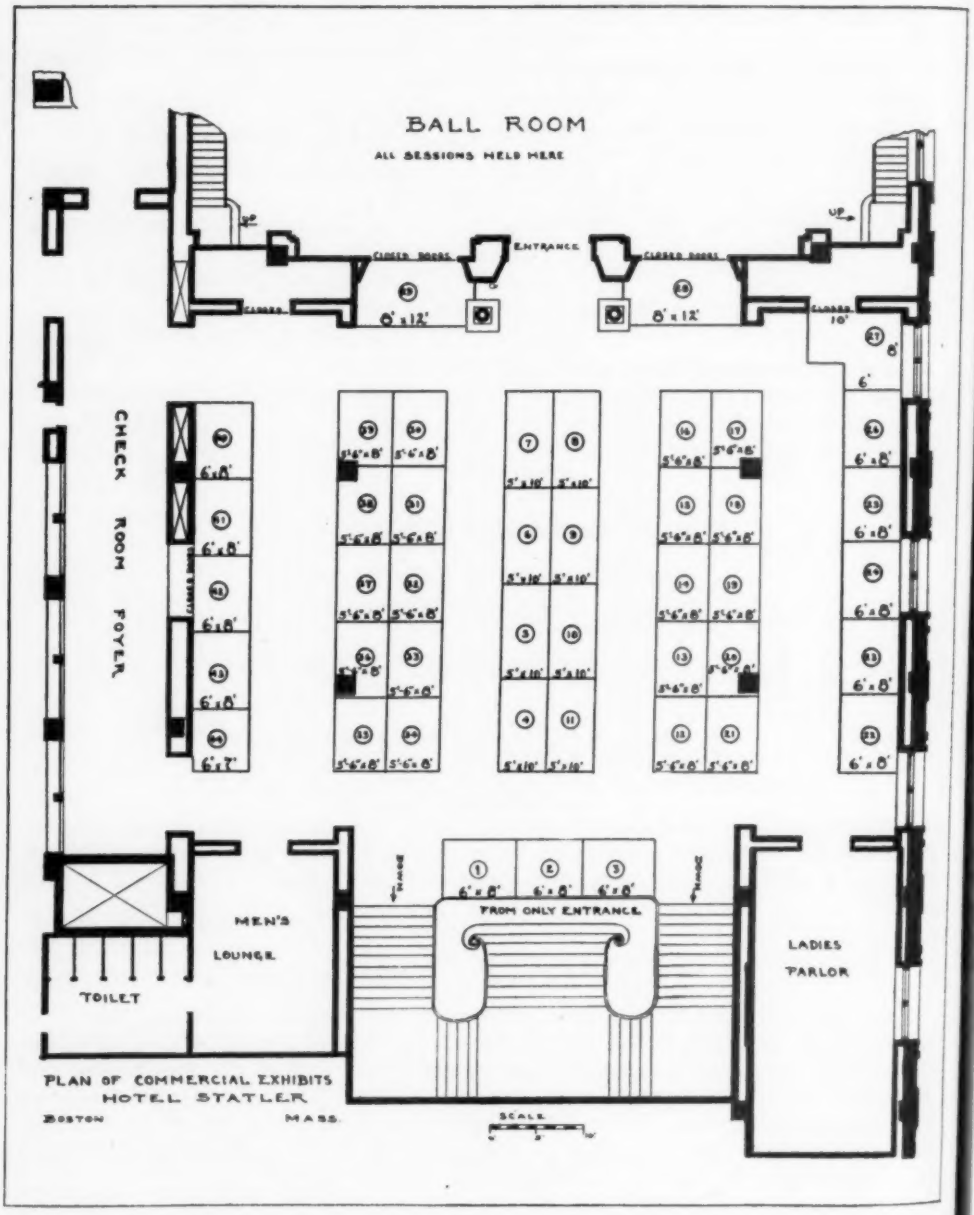
Program in charge of Capt. F. L. Pleadwell, M.C., U. S. N.

Presentation of medical cases in the conference room of the hospital each morning. Following this the group will be split up in sections of five. Each section will be in charge of a ward medical officer, and the balance of the morning will be devoted to ward rounds.

## TECHNICAL EXHIBIT

The technical exhibits have been arranged by the Executive Secretary, Mr. E. R. Loveland, and the following chart shows the arrangement of booths and the assignment to exhibitors from various parts of the country. The exhibits are highly diversified in their variety and will bring to the attendants at the Clinical Session, the latest and most improved equipment, the best pharmaceutical products, almost the whole library of medical publications and many other products of special interest to the Internist, Pediatrician, Neurologist, Psychiatrist, Radiologist and research worker.

This Exhibit is undoubtedly the best arranged and the most popular one that The College has yet had. The location is in the Ballroom Foyer where all attendants to the meeting will pass through the exhibits daily. The Joseph T. Griffin Decorating Company, of Louisville, Kentucky, who installed the exhibits for the American Medical Association, the Southern Medical Association and many other prominent medical societies, will be in charge of the booths and decorations.


BALL ROOM
ALL SESSIONS HELD HERE
ENTRANCE
CLOSED DOORS
CLOSED
UP
CHECK ROOM FOYER
MEN'S LOUNGE
TOILET
FROM ONLY ENTRANCE
LADIES PARLOR
PLAN OF COMMERCIAL EXHIBITS
HOTEL STATLER
BOSTON MASS.
SCALE

## LIST OF EXHIBITORS

| Space | Name | City and State | Product |
|---|---|---|---|
| 20 | Abbott Laboratories | North Chicago, Ill. | Pharmaceutical Products |
| 12 & 21 | D. Appleton & Company | New York, N. Y. | Medical Publications |
| 31 | The Battle Creek Food Company | Battle Creek, Mich. | Health Foods |
| 22 | Bausch & Lomb Optical Co. | Rochester, N. Y. | Microscopes, Photomicro & Projection Apparatus |
| 40 | P. Blakiston's Son & Co. | Philadelphia, Pa. | Medical Publications |
| 13 | The Borden Sales Company, Inc. | New York, N. Y. | Merrell Soule Infant Foods |
| 26 | Britesun, Inc. | Chicago, Ill. | Therapeutic Lamps |
| 25 | Cambridge Instrument Co., Inc. | New York, N. Y. | Electrocardiographs & Accessories, and other Physiological Instruments |
| 3 | Cameron's Surgical Specialty Co. | Chicago, Ill. | Electro-Diagnostic Surgical & Dental Instruments |
| 44 | G. W. Carnrick Co. | Newark, N. J. | Pharmaceutical Products |
| 1 | Warren E. Collins, Inc. | Boston, Mass. | Roth-Barach Oxygen Apparatus |
| 14 | F. A. Davis Company | Philadelphia, Pa. | Medical Publications |
| 16 | Deshell Laboratories, Inc. | Chicago, Ill. | "Petrolagar" |
| 42 & 43 | General X-Ray Company | Boston, Mass. | "Morse" Wave Generator, GX-Galvine-Faradie Plate, Diathermy Apparatus, Electrodes |
| 34 | Paul B. Hoeber, Inc. | New York, N. Y. | Medical Publications |
| 19 | Horlick's Malted Milk Corporation | Racine, Wis. | Malted Milk Products |
| 17 | Kalak Water Company, Inc. | New York, N. Y. | Kalak Water |
| 4 | Charles B. Knox Gelatine Co., Inc. | Johnstown, N. Y. | Knox Gelatine |
| 15 | Lavoris Chemical Company | Minneapolis, Minn. | "Lavoris" |
| 45 | LaMotte Chemical Products Co. | Baltimore, Md. | LaMotte Blood Chemistry Outfits |
| 30 | Lea & Febiger | Philadelphia, Pa. | Medical Publications |
| 9 | J. B. Lippincott Company | Philadelphia, Pa. | Medical Publications |

| | | | |
|---|---|---|---|
| 29 | MacGregor Instrument Company | Needham, Mass. | Vim Stainless Steel Needles; Vim Emerald Luer Syringes; Vim Surgical & Medical Specialties |
| 8 | The Macmillan Company | New York, N. Y. | Medical Publications |
| 2 | E. F. Mahady Company | Boston, Mass. | Anaesthetic Apparatus, Laboratory Equipment, Diagnostic & Scientific Apparatus, Vaccines, Intravenous Products, Orthopedic Appliances & Supplies, Instruments for Operating Room, E.F.M. Catgut |
| 18 | The Medical Protective Company | Chicago, Ill. | Malpractice Insurance |
| 24 | Mellin's Food Company | Boston, Mass. | Mellin's Food |
| 38 | Merck & Company, Inc. | Rahway, N. J. | Pharmaceutical Products |
| 23 | The Wm. S. Merrell Company | Cincinnati, Ohio | Pharmaceutical Products |
| 32 & 37 | Merrell Soule Company | New York, N. Y. | Infant Foods |
| 35 | The C. V. Mosby Company | St. Louis, Mo. | Medical Publications |
| 39 | Thomas Nelson & Sons | New York, N. Y. | Medical Publications |
| 28 | The E. L. Patch Company | Boston, Mass. | Cod Liver Oil |
| 6 | Pittsburgh Plate Glass Co. | Pittsburgh, Pa. | "Helioglass" |
| 7 | Richards, Inc. | Glenolden, Pa. | Psyllium Seed & Acidophilus Products |
| 11 | W. B. Saunders Company | Philadelphia, Pa. | Medical Publications |
| 27 | Sanborn Company | Cambridge, Mass. | "Graphic" Metabolism Apparatus |
| 41 | Spencer Lens Company | Boston, Mass. | Optical Instruments, Projection Apparatus, Laboratory Equipment |
| 50 | Swan-Myers Co. | Indianapolis, Ind. | Pollens, Ephedrine Preparations, Dextrose Ampoules and other Pharmaceutical Products |
| 36 | Tailby-Nason Company | Boston, Mass. | Cod Liver Oil |
| 5 & 10 | Victor X-Ray Corporation | Chicago, Ill. | Electrocardiograph & Quartz Lamps |
| 33 | Winthrop Chemical Company, Inc.<br>H. A. Metz Laboratories, Inc. | New York, N. Y. | Pharmaceutical Products |

## THE MACMILLAN COMPANY

Booth 8

The Macmillan Company will display at Booth 8 a long list of recent and important medical books for the Internist. There are few other opportunities when one may leisurely look over the medical publications, past and recent, as at the Exhibit of this Clinical Session. Macmillan's announcements may also be found on page one of the Advertising Section of this journal.

## MERRELL SOULE COMPANY

Booths 32-37

Merrell-Soule Powdered Protein Milk is the dehydrated equivalent of Finkelstein's original Eiweissmilch and should not be confused with calcium caseinate or other preparations used in preparing a formula high in protein. The removal of a large proportion of the whey and retention of the lactic acid producing organisms in a viable condition contributes very largely to the product's therapeutic value. The wealth of clinical evidence accumulated in recent years compels us to submit that protein milk, as well as being ideal for, is the food of choice for the premature infant and for those types of nutritional disturbances characterized by hydrolability and inability to digest or assimilate normal formulae with consequent failure to gain. Samples and literature may be obtained by calling at the booths of the Merrell-Soule Company at the Exhibit during the Clinical Session.

## LEA & FEBIGER

Booth 30

At Booth 30, Lea & Febiger will exhibit medical books of all descriptions, several by Fellows of The College. Orders may also be placed with them for subscription to the oldest medical journal in America devoted to Medicine, *The American Journal of Medical Sciences*. Lea & Febiger's announcements of publications may be found on page 8 of the Advertising Section of this journal.

## DASHELL LABORATORIES, INC.

Booth 16

Petrolagar, the emulsion for use in place of plain mineral oil will be interestingly displayed at the meeting in Boston, April 8-12.

## KALAK WATER COMPANY

Booth 17

The Kalak Water Company will exhibit at Booth 17 "Kalak Water," made of distilled water and chemically pure salts of the kind normally present in the body. Kalak Water is non-laxative and higher in available alkali and richer in Calcium than any natural or artificial water known.

## D. APPLETON & COMPANY

Booths 12-21

A long list of important medical books and publications will be exhibited at the double booth of D. Appleton & Company, where will be found a number of courteous men fully conversant with the field of medical publications to give you information and to show you the publications of this Company.

## THE BATTLE CREEK FOOD COMPANY

Booth 31

"Lacto-Dextrin," a special colon food for changing the intestinal flora to combat autointoxication, will be one of the products exhibited at Booth 31 by The Battle Creek Food Company. Their various pamphlets concerning all of their products will be gladly sent upon request.

## BAUSCH & LOMB CO.

Booth 22

Among the most important instruments which are universally used in the physician's laboratory throughout the world is the microscope. It has become a necessity for the study of bacteriology and pathology, for the making of bloodcounts and performing numerous other functions which make the medical practice what it is today.

Because of its fine resolution and high magnification, the Bausch & Lomb FFSA-8 Microscope is the instrument which enjoys the greatest popularity and has been chosen by the members of the medical profession as their laboratory instrument. This "Physicians' Microscope," as it is popularly designated, is an ideal instrument for bacteriological work. Its 43X (4mm) long working distance objective is unequalled for work with the haemacytometer.

The FFSA-8 is provided with a 10X and a 43X objective and a 97X oil immersion objective for high power work. These objectives together with the 5X and 10X huygenian eyepieces furnish a range from fifty to about one thousand times. Each of these objectives is mounted in standardized mounts, the lens elements being exactly set in threadless cells, so that precise centering of the lens element is assured.

The latest improvement of this Physicians' Microscope is the built-on mechanical stage which is indispensable in blood counting and offers a means for systematically examining a 50 by 75mm slide.

The FFSA-8 is regularly equipped with a divisable Abbe condenser, B & L Patented side fine adjustment and an improved rack and pinion substage.

This microscope is to be on exhibition at the meeting of The American College of Physicians in April, 1929. A detailed explanation and demonstration will be given at that time.

## THE WM. S. MERRELL COMPANY

Booth 23

Among products exhibited by The Wm. S. Merrell Company will be "Lacricin," described as "milk of castor oil." This product is a thick creamy substance, perfectly emulsified, looking and tasting like whipped cream, but retaining the full effects of the castor oil, without its taste. Undoubtedly, such a product will find a warm welcome among physicians and patients other than children, for it happens all too often that a salt or pill is surreptitiously substituted for the castor oil prescription, even where the latter may be essential for correct results. Lacricin can be prescribed without the patient being aware of the fact that he (or in the obstreperous case probably more often "she") is to take castor oil.

"It's Not the Cost—It's the Upkeep" is the title of an amusing little circular recently issued by The Wm. S. Merrell Company, depicting graphically the numerous "bribes" offered by fond parents to their unruly offspring refusing to take the "nasty castor oil" that the doctor prescribed.

## P. BLAKISTON'S SON & CO.

Booth 40

*P. Blakiston's Son & Co., Publishers, Philadelphia,* will exhibit in Space No. 40 their publications on Medicine and Allied Sciences, including some Englsh books and translations of some desirable foreign volumes. Special attention is directed to Kaufmann's "Pathology," 3 Volumes, translated by Reimann; Fulkerson "Text-book of Gynecology"; Deaver's "Surgical Anatomy," 2nd Edition; Riehl & Von Zumbusch "Atlas of Diseases of the Skin"; "Recent Advances Series"; Smith "Forensic Medicine," 2nd Edition; Stitt "Tropical Diseases," 5th Edition; Halliburton "Physiology," 18th Edition; Gould's "New Medical Dictionary," 2nd Edition.

LAMOTTE CHEMICAL PRODUCTS CO.

BOOTH 45

LaMotte Blood Chemistry outfits offering simplified blood chemistry methods for the general practitioner as well as the technician will be displayed in a full line at Booth 45. Although the chart on a preceding page does not show this booth, so great has been the demand for exhibit spaces that additional booths have been arranged along the check room foyer, where the LaMotte Chemical Products Company has engaged a prominent location.

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At the last annual session of the Southern Medical Association at Asheville, North Carolina, Dr. Felix J. Underwood (Fellow), State Health Officer for Mississippi, was elected Second Vice President; Dr. William R. Bathurst (Fellow), Little Rock, Ark., Chairman of the Board of Trustees; and Dr. W. S. Leathers (Fellow), Nashville, Tenn., Dr. Stewart R, Roberts (Fellow), Atlanta, Ga., and Dr. Charles C. Bass (Fellow), New Orleans, La., were elected members of the Board of Trustees.

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Dr. V. P. Sydenstricker (Fellow), Augusta, Georgia, gave a medical clinic and Dr. William A. Mulherin (Fellow), Augusta, Georgia( gave a pediatric clinic before the Sixth District Medical Society at Macon, Georgia, on November 28.

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Dr. William R. Dancy (Fellow), Savannah, Georgia, is President-Elect of the Medical Association of Georgia; Dr. Allen H. Bunce (Fellow), Atlanta, is Secretary-Treasurer.

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Dr. Morris H. Kahn (Fellow), New York City, recently delivered a lecture before the Lackawanna County Medical Society in Scranton, Pa., on the subject "The Industrial Aspects of Heart Disease."

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Dr. John H. Musser (Fellow and President-Elect), New Orleans, addressed the Issaquena-Sharkey-Warren Counties Medical Society at Vicksburg, Mississippi, December 11, on "Throat Infections in General Medicine."

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Dr. W. McKim Marriott (Fellow and Third Vice President), St. Louis, addressed the section on Pediatrics of the New York Academy of Medicine, January 3, on "The Clinical Aspects of the Rôle of Focal Infections in producing Gastro-intestinal Symptoms in Infants and Children."

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Dr. Thomas Noxon Toomey (Fellow), St. Louis, addressed the Lee (Iowa) County Medical Society at Fort Harrison, December 20, on "Pruritus and Dermatitis of Internal Origin."

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Dr. George B. Eusterman (Fellow) Rochester, Minn., spoke before the Rice County (Minnesota) Medical Society at Northfield, November 26, on the subject "Appraisal of New Methods in the Diagnosis of Cholecystic Disease."

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Dr. John G. Ryan (Fellow) of Denver, Colo., has recently become a Life Member through subscription to the Endowment Fund or The American College of Physicians.

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Dr. H. M. Eberhard (Associate), Philadelphia, Professor of Gastro-Enterology at Hahnemann Medical College, recently described in detail "The Ionization of Zinc Sulphate in Chronic Colitis" in a clinic at the College.

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Dr. George B. Lake (Associate), Managing Editor of "Clinical Medicine and Surgery," North Chicago, Ill., addressed the Lee County, Iowa, Medical Society, at Fort Madison, December 20, 1928, his subject being "Psychic Factors in Disease."

A small volume of Dr. Lake's verses, "An Apostle of Joy," came out in December (Northshore Publishers, Highwood, Ill,), and articles of his appeared in the November "Welfare Magazine"; November and December "Medical Economics"; November and December "Hospital Topics and Buy-

er"; and a verse in the November "Step Ladder." He was also reëlected editor of *The Bulletin* of the Medical Round Table of Chicago at the annual meeting of that organization.

Dr. Cyrus W. Strickler (Fellow), Atlanta, Ga., addressed the Fulton County Medical Society at Atlanta on December 6 on "Precordial Pain Simulating Angina Pectoris."

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Dr. Carl J. Wiggers (Fellow), Cleveland, December 3, delivered the Chaille Memorial Oration before the Orleans Parish Medical Society at New Orleans.

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Dr. Carl V. Vischer (Fellow), Philadelphia, is author of an article in the January 1929 issue of The Hahnemannian Monthly entitled "The Management of the Chronic Tuberculous Patient."

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Dr. Charles W. Stone (Fellow), Cleveland, addressed the Eighth District Medical Society at Nelsonville, Ohio, November 1, on "The Modern Trend." Dr. Stone is president of the state medical society.

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Dr. E. Bates Block (Fellow), Atlanta, delivered an address on "Treat the Mind as Well as the Body" before the Kings County Medical Society, New York, on November 16.

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Dr. Logan Clendening (Fellow), Kansas City, at a meeting of the Jackson County (Mo.) Medical Society commemorating the tercentenary of Dr. William Harvey's publication of De Motu Cordis, November 27, spoke on "The Life and Labor of William Harvey."

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Dr. Max Einhorn (Fellow), New York, was one of the speakers at the inauguration of the lectures of the International Spanish Speaking Association of Physicians, Dentists and Pharmacists on November 27.

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Dr. Charles W. Burr (Fellow), Philadelphia, addressed the section on medical history of the Philadelphia College of Physicians, December 4, on "Dr. Robert Whytt and Internal Hydrocephalus."

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Dr. James Marr Bisaillon (Fellow), Portland, Oregon, addressed the Klickitat-Skamania Counties Medical Society, October 18, at White Salmon, Oregon, on "Mistakes in Diagnosis of Tuberculosis."

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Dr. Austin B. Jones (Fellow), Kansas City, addressed the Clay County (Mo.) Medical Society, October 25, on "Diagnosis and Treatment of Cardiac Disorders."

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Dr. James M. Anders (Master), Philadelphia, November 24, spoke before the Association of College Presidents of Pennsylvania, Harrisburg, on "The Research Method of Teaching."

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Dr. Lawrence Selling (Fellow), Portland, Oregon, read a paper before the Central Willamette Medical Society in November, entitled "Changes in our Views of Neuroses."

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Dr. Oliver K. Kimball (Fellow), Cleveland, addressed the Muskegon County Medical Society at its October meeting on "Prevention of Goiter Among School Children."

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Dr. William C. Rucker (Fellow), New Orleans, was guest of honor at the annual banquet of the Orleans Parish Medical Society in December.

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Dr. John Walker Moore (Fellow), Louisville, has assumed the duties of Dean of the School of Medicine of the University of Louisville, succeeding Dr. Stuart Graves (Fellow), who has become Dean of the University of Alabama, School of Medicine, at Tuscaloosa.

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Dr. Cyrus C. Sturgis (Fellow), Ann Arbor, spoke before the Shiawassee County (Michigan) Medical Society at its November meeting on heart disease.

Dr. Sturgis also addressed the Milwaukee County Medical Society on November 9.

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Dr. James L. Bibb (Fellow), Chatta-

nooga, has been elected President of the East Tennessee Medical Association for 1929.

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Dr. Emanuel Libman (Fellow), New York, addressed the Kings County Medical Society, December 18, on "Some Phases of Rheumatic Fever."

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Dr. Frank Smithies (Fellow), Chicago, addressed the Marquette-Alger Counties Medical Society, November 3, on "Gastric Hemorrhage, Its Significance and Treatment."

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Dr. Gerald B. Webb (Fellow), Colorado Springs, will address the medical section of the American Association for the Advancement of Science during its annual session on "The Rôle of Physicians as Poets and Men of Letters."

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Rear Admiral Edward R. Stitt (Fellow), Surgeon General of the United States Navy, retired voluntarily at the close of his second full term on November 30. Admiral Stitt was appointed Surgeon General by President Wilson on November 26, 1920, and was re-appointed by President Harding and President Coolidge. He has left Washington for duty as general inspector of activities of the Naval Medical Department on the Pacific Coast and in Hawaii.

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A bill has been introduced in the United States Senate by Senator Bruce to authorize Dr. William S. Thayer (Fellow), Baltimore, "to accept such decorations, orders and medals as have been tendered him by foreign governments." Government authority is necessary before members of the Medical Reserve Corps of the Army can accept foreign decorations.

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Dr. Robert M. Moore (Fellow), Indianapolis, addressed the November meeting of the Ft. Wayne County Medical Society on heart disease.

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Dr. Frederick Epplen (Fellow), Seattle, conducted, on November 13, a pathological confeernce before the Walla Walla Valley Medical Society. He presented specimens to illustrate obscure ulcerative and malignant conditions.

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Dr. Arthur F. Chace (Fellow), New York, was one of the speakers on January 9 at a testimonial dinner to Dr. James McKernon at his retirement as President of the New York Postgraduate Medical School and Hospital.

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Dr. Edward B. Krumbhaar (Fellow), Philadelphia, was recently elected President of the Rush Society of the University of Pennsylvania.

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Dr. Orlando H. Petty (Fellow), Philadelphia, spoke before the Montgomery County (Pa.) Medical Society, November 7, on diabetes.

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Dr. Warfield T. Longcope (Fellow), Baltimore, Professor of Medicine at the Johns Hopkins Medical School, was one of the speakers at the dedicatory exercises, December 5, of the new dispensary and outpatient department of the Johns Hopkins University Medical School.

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Dr. David Riesman (Fellow), Philadelphia, delivered an illustrated lecture on "Prehistoric Man" before the Brooklyn Institute of Arts and Sciences at the Academy of Music, January 5.

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Dr. F. M. Pottenger (Fellow), Monrovia, Calif., presented a paper on "Disturbances in the Vegetative Nervous System in Diseases of the Lungs and Visceral Pleura" before the Association for Research in Nervous and Mental Disease, at its Ninth Annual Meeting, December 27-28, 1928, at the Hotel Commodore, New York City.

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Dr. Edwin Henes, Jr. (Fellow), Milwaukee, is engaged in editing and publishing the Atlanta 1928 Proceedings Volume of the Inter-State Post Graduate Medical Association of North America. This Volume will contain about one hundred articles (clinics and papers) contributed by about seventy of the leading physicians and sur-

geons of America and Europe. Most of the medical contributors, it is reported, are members of The American College of Physicians.

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Dr. V. C. Rowland (Fellow), Cleveland, has been elected Vice President of the Academy of Medicine of Cleveland. For a considerable period of time, Dr. Rowland has been Editor of the Bulletin of the Academy, and Chairman of the Ohio State Medical Association Committee on Periodic Health Examinations.

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Dr. Estella G. Norman (Fellow), Battle Creek, Michigan, on January 3 was reappointed as a member of the Michigan Board of Registration of Nurses and Trained Attendants by Fred W. Green, Governor of the state.

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Dr. W. S. Leathers (Fellow), Dean, Vanderbilt University Medical School, Nashville, addressed a meeting at the Rutherford Hospital, Murfreesboro, December 6, on "The Hospital in Relation to the Community."

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Dr. J. Gurney Taylor (Fellow), Milwaukee, was elected President of the Central States Pediatric Society at its recent annual meeting in Pittsburgh.

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Secretary Wilbur nominated, on December 26, 1928, Capt. Charles E. Riggs as Surgeon General of the Navy and Chief of the Bureau of Medicine and Surgery to succeed Rear Admiral Edward R. Stitt (Fellow), who has been transferred to the Pacific Coast to assume charge of the Navy's Medical activities there and in Hawaii. Capt. Riggs has been in command of the Naval Hospital at Washington.

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Dr. E. J. G. Beardsley (Fellow), Philadelphia, addressed the first Graduate Fortnight of the New York Academy of Medicine on "Practical Preventive Medicine."

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### Gifts to The College Library

Acknowledgment has been made of the following recent gifts to The College Library:

By Dr. F. M. Pottenger (Fellow), Monrovia, Calif.
- Book, "Muscle Spasm and Degeneration"
- Book, "Tuberculin in Diagnosis and Treatment"
- Book, "Tuberculosis and How to Combat It"
- Book, "Symptoms of Visceral Disease, 3d edition
- Book, "Clinical Tuberculosis," Vol. I, 2d edition
- Book, "Clinical Tuberculosis," Vol. II, 2d edition

By Dr. Raymond J. Reitzel (Associate), Galveston, Texas.
- Reprint, "Lobar Pneumonia in Negroes: The Influence of Syphilis as a Coexisting Disease"
- Reprint, "The Effect of pH on the Oxygen Consumption of Tissues"
- Reprint, "Parathyroid Extract—Collip as a Diuretic"
- Reprint, "Liver Diet in the Treatment of Severe Anemia"

By Dr. Philip B. Matz (Fellow), U. S. Veterans Bureau, Washington, D. C.
- Reprint, "Diseases of the Skin Among Ex-Service Men"
- Reprint, "The Tuberculosis Problem in the United States Veterans Bureau"

All members are urged to donate copies of their own publications to the College Library, which is intended to be a memorial library and a directory of the publications of our Associates, Fellows and Masters.

## OBITUARY

*Dr. Charles Launcelot Minor*

When Charles Launcelot Minor, M.D., LL.D., specialist in tuberculosis and brilliant writer, died at his home in Biltmore Forest, N. C., in his sixty-fourth year Wednesday morning, December 26, 1928, the medical profession and The American College of Physicians lost a member who had achieved national and international fame.

Although he had suffered from heart trouble for several years, his death came suddenly. He died at eight o'clock in the morning, a few minutes after he had begun to dress for breakfast.

Dr. Minor ranks with Trudeau in discovering and disseminating the treatment of tuberculosis. He was generally credited with having been the first physician to realize the importance of the psychological element in the management of tuberculous patients. He was a pioneer in perfecting the method of making physical examinations, which he early considered as important as laboratory tests.

After securing his medical degree at the University of Virginia in 1888, Dr. Minor was house physician in St. Luke's Hospital in New York, 1888-1890. He then went abroad, doing postgraduate work in Berlin, Dublin, London, Paris and Vienna. Returning to this country, he began the general practice of medicine in Washington, D. C., but in 1895, having developed tuberculosis, he moved to Asheville, which was thereafter his home.

In studying his own case, he developed a deep interest in tuberculosis, and, having achieved a rapid recovery, began his career as a specialist in pulmonary diseases. His success was pronounced from the start. His reputation was soon established, and his fame became nation-wide.

He was not satisfied with giving his patients the results of his study and genius. He had a veritable passion for educating both the public and the medical profession in the best way to combat what was then called "the Great White Plague."

He wrote on the subject constantly and forcefully. His contribution on "Symptoms and Diagnosis of Tuberculosis" in Klebs' "Tuberculosis," published by D. Appleton and Company in 1908, still ranks as one of the greatest pronouncements on the subject in the English tongue.

He contributed many articles to both medical and lay journals, all for the purpose of spreading the gospel of the effective treatment of tuberculosis. His brochures on the subject are regarded as classics in medical literature.

Dr. Minor was also in great demand as a speaker before medical conventions. His eloquence and his thorough knowledge of his subject, combined with his forceful personality, gave him a tremendous acquaintance and popularity among the physicians and surgeons of this and other countries.

His eminence and success as a prac-

titioner were paid the tribute of many honors. He was president of the American Climatological and Clinical Association in 1916; president of the National Tuberculosis Association in 1918; president of the Southern Medical Association ni 1924. He was a member of the American Medical Association, the Association of American Physicians, and of other medical societies. He was governor for North Carolina of the American College of Physicians.

His constructive ability in his profession was matched by his activities in the life of his home town. He was a member of the Pen and Plate Club, the Civitan Club and the Biltmore Forest Country Club; the Colonade Club and the chapters of Delta Psi, Alpha Omega Alpha, and the Phi Beta Kappa fraternities at the University of Virginia.

He was a member and vestryman of Trinity Episcopal Church of Asheville. And with the same enthusiasm that he worked for the advancement of his church, he labored for the development and progress of his city.

No better description of Charles Launcelot Minor as a man can be found than the following paragraph from an editorial in "The Asheville Citizen" at the time of his death:

"But it is to his personality that his friends—and all Ashevillians were his friends—today pay the proudest and most loving tribute. Dr. Minor was a man beloved by his community. His unfailing charm, his flashing wit, his profound and versatile scholarship, his lively interest in all human affairs and his eagerness to be of service to all with whom he came in contact—these qualities of the man endeared him to our people to a degree of affection that seldom is given to anybody."

In 1926, when Dr. Minor was given the degree of Doctor of Laws by the University of North Carolina, the citation accompanying the award, written by Dr. Archibald Henderson, said:

"Charles Launcelot Minor, Asheville. Born in Brooklyn, N. Y., M.D., of the University of Virginia; later prosecuted detailed researches in medical science in England and on the continent. Through intimate association with the famous Viennese bacteriologist Klebs, to whose renowned book 'Tuberculose' he contributed an important chapter, he early turned the full current of his eclectic mentality upon the complex problems of tuberculosis, its diagnosis, treatment and prevention. Author of many authoritative scientific publications, chiefly devoted to the study of tuberculosis, he ranks today as an authority on that disease without a superior in the entire country. Versatile in attainments, eclectic in taste, like the late Dr. Weir Mitchell, he has, through the magic of his sympathetic and scintillating personality as well as by the depth of his knowledge and the range of his interests, won alike the unquestioned confidence and ardent devotion of his patients. Upon this scientific expert the University will now confer the degree of Doctor of Laws."

Funeral services for Dr. Minor were held the afternoon of December 27, 1928, at Trinity Episcopal Church in Asheville, with the Right Reverend Junius M. Horner, bishop of the dio-

cese, and the Rev. George Floyd Rogers, rector of Trinity, officiating. The body was then taken to New York, where interment was made in Greenwood Cemetery.

Although he received the greater part of his education in Virginia schools and at the University of Virginia, and though he was so thoroughly identified with the South, Dr. Minor was born in Brooklyn, N. Y., May 10, 1865. His parents were Dr. James Monroe Minor of Fredericksburg, Va., and Mrs. Ellen J. Pierrepont Minor of Brooklyn.

He is survived by his widow, who was Miss Mary McDowell Venable of Charlottesville, Va., and by three children, one of them a son, Dr. John Minor, now practising medicine in Washington, D. C.

Dr. Minor was a great physician and a great citizen. He loved men and he loved books. His loyalty to friends and to his community and country was limitless. His career may well serve as a guide to any man who wishes to achieve eminence ni his profession and worth to his fellows.

(Furnished by Dr. Thompson Frazer (Fellow), Asheville, N. C.)

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Dr. Jacob Wolf (Fellow), Pittsburgh, Pa., died November 19, 1928, at Atlantic City, N. J., of cerebral hemorrhage, aged 58.

Dr. Wolf was born in Union City, Tenn., educated in Cincinnati where he also graduated from the Medical College of Ohio in 1891. He then spent some time in postgraduate work in Europe and in 1894 came to Pittsburgh where he located on the North Side, eventually limiting his practice to internal medicine. At the time of his death, he was the senior member of the medical staff of the Allegheny General Hospital of Pittsburgh. He had been a Fellow of the College since 1920.

(Furnished by D. Lawrence Litchfield, Governor for Penn.)

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Dr. Eric Kline Bartholomew (Fellow), Chicago, Ill., died December 18, 1929, of epidemic cerebrospinal meningitis contracted from a patient.

Dr. Bartholomew received his medical degree from the University of Illinois, Chicago, in 1907. For several years he was assistant clinical professor of medicine at Loyola University School of Medicine; from 1914 to 1918 he was a member of the visiting staff of St. Mary's of Nazareth Hospital, and later was a member of the senior medical staff of the same institution. At the time of his death, he was also a member of the staff of the Lutheran Memorial Hospital. He was a member of the Chicago Medical Society, the Illinois State Medical Society and a Fellow of the American Medical Association. He was elected to Fellowship in The American College of Physicians April 3, 1922.

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Dr. Enoch H. Miller (Fellow), Liberty, Mo., died October 8, 1928, of influenza and broncho-pneumonia.

Dr. Miller was born in 1851, and received his medical degree from the Missouri Medical College, St. Louis, in 1874. He was a Fellow of the American Medical Association, a member of his county and state medical societies, and had been a Fellow of The American College of Physicians since December 27, 1924.

## 1929 COLLEGE DUES

The Executive Secretary, Mr. E. R. Loveland, 133-135 S. Thirty-sixth Street, Philadelphia, Pa., distributed the bills for 1929 dues at the beginning of January. A great majority of the members have already mailed their checks and have received their 1929 Membership Cards. Several, however, have not to date paid the dues, and are urged to do so immediately. The 1929 Membership Card is necessary to register at the Boston Clinical Session in April, and none but those in good standing will be entered on the subscription list to receive Volume III of Annals of Internal Medicine, the new Year Book and other publications. It will assist the Executive Secretary greatly if all dues are paid promptly.

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## THE ADVERTISING SECTION OF THIS JOURNAL

Members and Subscribers have noted the addition and successful growth of Advertising in Annals of Internal Medicine during the past few months. In April, 1928, The Board of Regents authorized the Executive Secretary to start the promotion of advertising, and appointed an Advertising Censorship Committee consisting of:

Dr. George Morris Piersol, Chairman
Dr. Harlow Brooks
Dr. E. J. G. Beardsley

The Committee and the Executive Secretary have worked diligently to build up a high-grade advertising clientele, and seeks to enlist the assistance of every member and subscriber in further promoting this section. The Advertising Section of Annals of Internal Medicine is valuable to the College for it helps to defray a part of the cost of publication, it is valuable to the reader because it announces only high grade products, apparatus and publications; and it must be lucrative to the advertiser to merit his continued patronage. It is known by the publishers that our members and subscribers do patronize our advertisers, but so frequently they do not mention the journal when placing orders or writing inquiries. To patronize our advertisers, to mention Annals of Internal Medicine, to recommend our advertising columns, are means of helping The College and of promoting the journal.

Annals of Internal Medicine, as the official journal of the American College of Physicians, has a *preferred circulation;* it arrives monthly at the offices of nearly two thousand eminent American internists, diagnosticians, pediatricians, psychiatrists, neurologists, radiologists, pathologists, bacteriologists, medical teachers and investigators, and tuberculosis and public health specialists. Its circulation is *national,* for it goes to every state and possession of the United States; it also goes to subscribers in Canada, Mexico and sixteen other foreign countries. Annals has attained, during its seven years of publication, an *eminence in American medicine,* excelled by no other journal devoted exclusively to Internal Medicine. The Advertising Section is limited to twenty pages in one issue, thus giving prominence for each advertisement, and therefore no advertisement is lost in a great host of other advertising. Furthermore, only high grade advertisements are accepted, each tendered advertisement passing review by the Censorship Committee.

Patronize our advertisers and use your influence with other organizations, whose advertising does not already appear in this journal, to adopt *Annals* as a medium for continuous advertising.

# Boston As A Medical Center

By Henry A. Christian, M.D.

THE student of medicine who comes to Boston finds himself with access to modern, well equipped hospitals and medical laboratories. There is a wealth of clinical material, freely accessible to graduate and undergraduate medical students. Three excellent medical schools offer a large variety of medical courses. A splendid medical library hospitably invites the reader to use its fine collection of medical books.

In Boston, a city rich with traditions of able men and significant events, medicine, too, has its honored traditions. Here was established in 1782 one of the earliest American medical schools, from its inception an integral part of a university. In Boston in 1811 was founded the Massachusetts General Hospital one of our early hospitals, which since its opening in 1821 has never closed its doors to patients. At the Massachusetts General Hospital on October 16, 1846 was performed that major surgical operation under ether anaesthesia, which more than anything else served to abolish pain from surgical procedures and made possible an ever increasing scope to surgical practice.

Founded in 1782 the Harvard Medical School occupied buildings of Harvard College in Cambridge until 1819, when it was moved to Boston to secure better clinical opportunities for its students. In 1816, 1847, 1882, and 1906, respectively, special buildings were constructed in Boston for its use. In these a succession of eminent men have labored in the cause of medical education. The Warren family from the days of the battle of Bunker Hill has held a commanding position in Boston. Dr. Joseph Warren played an important rôle in the Revolutionary War. His brother John Warren was Harvard's first professor of Anatomy and Surgery and since 1782, with but a brief interregnum, until last year, a Warren has held a professorial chair at Harvard. It was a Warren (John Collins Warren) who performed at the Massachusetts General Hospital that all significant operation under ether anaesthesia given at the hands of W. T. G. Morton. Oliver Wendell Holmes, essayist, poet and professor of Anatomy gave the name, anaesthesia, to the process. Holmes' paper on puerperal fever was a very important step in bringing about a general acceptance of the contagiousness of that disease. Benjamin Waterhouse, first professor of the Theory and Practice of Physic, was a Leyden graduate and played an important role in the introduction into America of vaccination against small pox. In July, 1800 he vaccinated first of all his

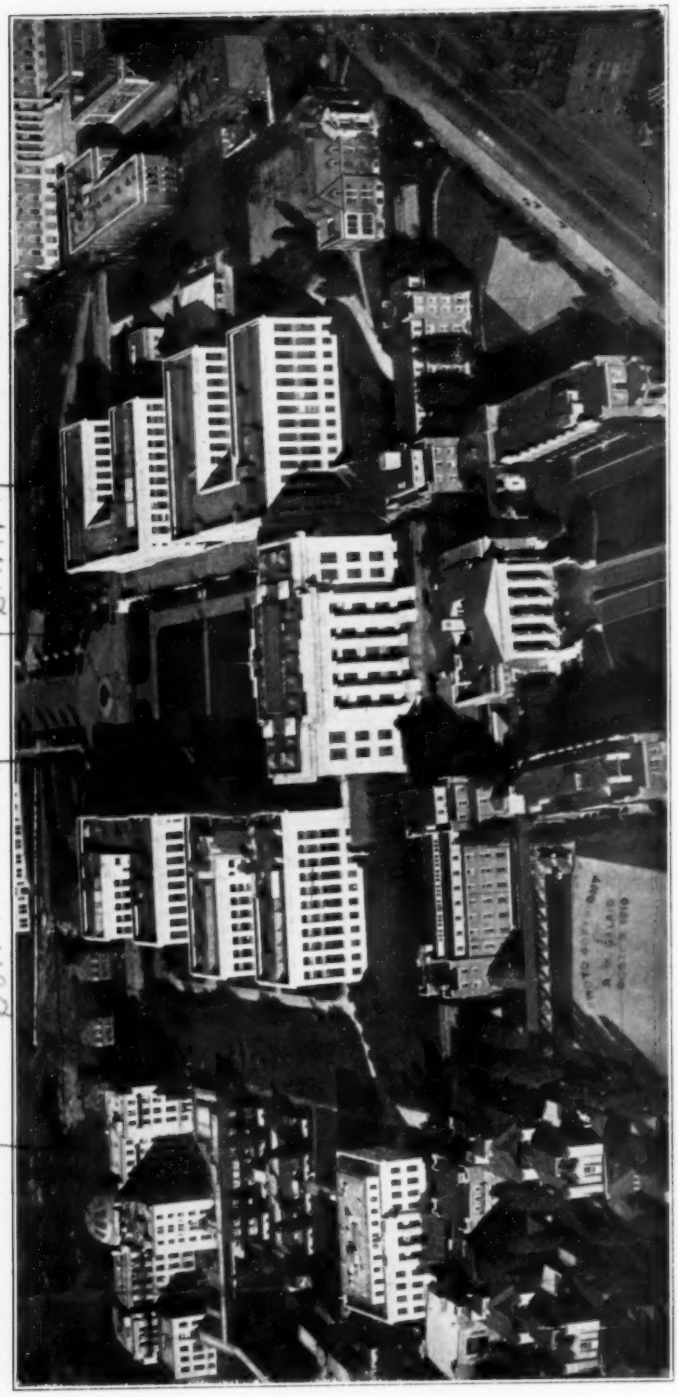

FIG. 1. HARVARD MEDICAL SCHOOL, AIR-PLANE VIEW. HARVARD MEDICAL SCHOOL, CENTER GROUP OF WHITE BUILDINGS. IN FOREGROUND, PART OF PETER BENT BRIGHAM HOSPITAL. AT LEFT, WHITE BUILDING IS HARVARD SCHOOL OF PUBLIC HEALTH. BEYOND THIS ON LEFT ARE BUILDINGS OF CHILDREN'S HOSPITAL. ON RIGHT IS HUNTINGTON MEMORIAL HOSPITAL AND HARVARD DENTAL SCHOOL.

Fig. 2. Tufts College Medical School.

son and later others. At a subsequent date Dr. Waterhouse received from Jenner a silver snuff box containing vaccine inscribed "Edw. Jenner to B. Waterhouse." James Jackson with Warren was a founder of the Massachusetts General Hospital and a very outstanding medical man of his time whose "Letters to a Young Physician" are classic. Jacob Bigelow, Harvard's first professor of materia medica, recognized and taught the self limitation of many infectious diseases. Henry J. Bigelow, a striking figure in surgery, described the Y-ligament and showed its importance in the reduction of dislocations of the hip. David W. Cheever, a remarkable lecturer, taught many students from his store of surgical wisdom. Henry P. Bowditch developed the first laboratory of physiology in this country and in it trained many of the men who subsequently organized departments of physiology in American medical schools. Theobald Smith, professor of Comparative Pathology, demonstrated insect transmission of disease. Reginald Heber Fitz proved that the appendix is the most frequent point of origin of peritonitis and suggested the term "appendicitis," while a colleague, Maurice H. Richardson, spread the gospel of the importance of early operation in appendicitis. Fitz' work on pancreatitis also was of the pioneer type. A son, as Associate Professor of Medicine at Harvard, perpetuates his name in its medical associations. The Shattucks form another family group who have played an important rôle in Boston medicine. A Shattuck endowed the chair of pathological anatomy at Harvard in 1846, his son and grandson were professors in the departments of Medicine and wise practitioners of their time, teaching both the art and the science of medicine, and a great grandson at present serves the school as assistant professor of Tropical Medicine. Richard C. Cabot at the Massachusetts General Hospital originated medical social service work. These and many others, in the years

Fig. 3. Beth Israel Hospital.

since 1782, have built up for Boston truly an inspiring tradition of medicine.

Three important medical schools are located in Boston, the Harvard Medical School, (Fig. 1), founded in 1782, Boston University School of Medicine founded in 1873 and Tufts College Medical School founded in 1893. The first medical school for women in the United States was founded in Boston in 1848 as the New England Female Medical College. In 1873 this became the Medical Department of Boston University.

In 1927-28 there was an enrollment at Harvard of 521 candidates for the M.D. degree and 439 graduate students, at Boston University of 205 candidates for the M.D. degree and at Tufts of 489 candidates for the M.D. degree. The Medical School budget for the 1927-28 session was as follows, Harvard $748,870.07, Boston University $138,000.00, Tufts College $149,095.18. In addition to the Medical School, Harvard has a school of Public Health with 26 enrolled students and a budget of $214,309.19 in 1927-28. Both Boston University and Tufts College Medical Schools have building programmes which before many years will give to these institutions greatly improved facilities for medical instruction. The latter plans to move the work of the first two years to Medford where the collegiate department is and there to house the medical students in dormitories.

Boston possesses a large group of hospitals of first rank, well equipped for the care of patients and possessed of laboratory facilities making possible

Fig. 4. Boston City Hospital. Front view of the Out-Patient Department.

a wide range of medical investigations. In these hospitals the education of medical students, physicians and nurses is being carried on throughout the year. These hospitals cooperate with the medical schools in such a generous way that in Boston there has never been the need for university owned hospitals. This has brought about for the medical schools an enormous saving in expenditure for clinical facilities and allowed the medical schools to concentrate their resources on the budget for labora-

FIG. 5. BOSTON CITY HOSPITAL. SIDE VIEW OF THE NEW SURGICAL BUILDING.

tories, instruction and investigation. Medical schools and hospitals have cooperated in making staff appointments so that the schools have freedom of selection of clinical teachers and the hospitals have profited by having added to their staffs, men eminent in their branch of medicine, freely selected from the country at large. Large clinical staffs in the various hospitals greatly reduces the burden of teaching put upon individual members of medical school departments. The spirit of whole hearted cooperation between hospitals and schools in Boston has been a great

FIG. 6. BOSTON CITY HOSPITAL. FRONT VIEW OF THE THORNDIKE MEMORIAL LABORATORY.

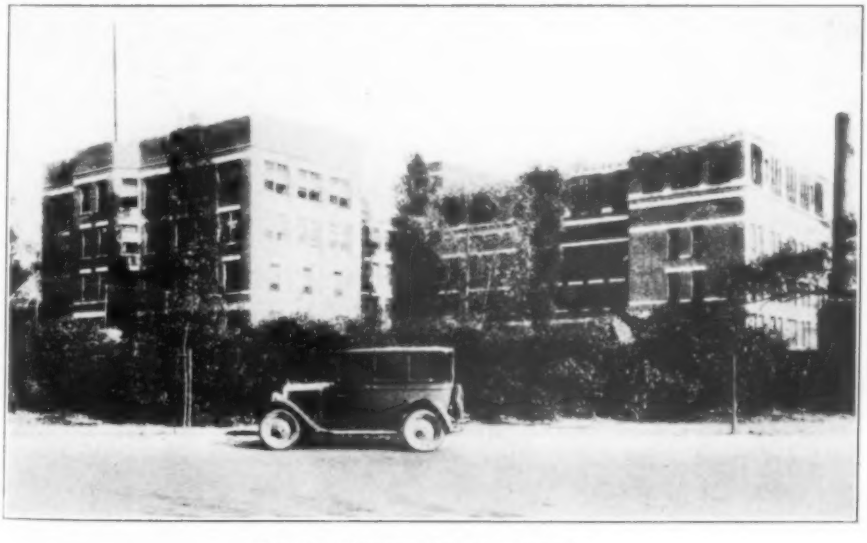

FIG. 7. PSYCHOPATHIC HOSPITAL.

FIG. 8. CARNEY HOSPITAL.

factor in developing Boston into one of America's leading medical centers.

The following brief statements about Boston's larger hospitals will serve to give some idea of the clinical facilities used here in medical teaching.

Beth Israel Hospital, (Fig. 3), recently constructed at a cost of $3,000,000, has 180 beds. This is a general hospital with a variety of services.

The Boston City Hospital, (Figs. 4 and 5), is a general hospital with 1891 beds covering a variety of services. There is also a large Out-Patient Department where last year 81,728 new patients came for treatment. In connection with the hospital the Thorndike Memorial Laboratory, (Fig. 6), furnishes extensive facilities for medical investigation. The South Department of the Boston City Hospital cares for contagious diseases and has a capacity of 338 beds where last year 2,380 cases were treated. Under the Boston City Hospital's direction is a large hospital at Mattapan for the treatment of tuberculous patients with the capacity of 422 beds.

The Boston Dispensary maintains a very large Out-Patient Department with 131,231 visits during the past year. In addition there is a well equipped hospital for children with 32 beds chiefly for medical cases.

The Boston Lying-in Hospital has 100 beds and during last year treated 2089 patients of whom 1715 were delivered. In addition in the Out-Patient Department 1250 cases were attended.

The Boston Psychopathic Hospital, (Fig. 7), is a state institution for acute, curable, incipient and doubtful cases of mental disease. It has 110

FIG. 9. CHILDREN'S HOSPITAL: ADMINISTRATION BUILDING.

FIG. 10. CHILDREN'S HOSPITAL, BIRD'S EYE VIEW.

Fig. 11. Free Hospital for Women.

beds and receives patients at the rate of about 1800 a year. There is also a large Out-Patient Department in connection with the hospital.

The Carney Hospital, (Fig. 8), is a general hospital with 220 beds and a large Out-Patient Department.

The Children's Hospital, (Figs. 9 and 10), has 244 beds where 5629 cases were treated last year. It has also a large Out-Patient Department in which 57,153 visits were made.

The Free Hospital for Women, (Fig. 11), is devoted exclusively to the surgical treatment of diseases peculiar to women. It has a capacity of 94 beds and a large Out-Patient Department.

The House of the Good Samaritan is a chronic hospital for the care of women and children particularly those with chronic heart disease and cancer. It has 75 beds.

The Infants' Hospital is adjacent to and under the management of the Children's Hospital. It has 66 beds for the care of infants.

Massachusetts Eye and Ear Infirmary, (Fig. 12), has 290 beds for the care of patients with diseases of the eye and ear. There is also a large Out-Patient service where in 1927 there were 73,624 visits.

The Massachusetts General Hospital, (Fig. 13), has 520 beds for general medical, surgical and pediatric cases; in addition there are special services for skin, orthopedics, laryngology, neurology, etc. Its large Out-Patient Department treated last year 31,871 new patients. The hospital also has extensive laboratories for special

FIG. 12. MASSACHUSETTS EYE AND EAR INFIRMARY.

FIG. 13. MASSACHUSETTS GENERAL HOSPITAL. BULLFINCH BUILDING IN THE DOME OF WHICH ETHER WAS USED IN MAJOR SURGERY ON OCTOBER, 16, 1846.

Fig. 14. New England Deaconess Hospital.

Fig. 15. Palmer Memorial Hospital.

Fig. 16. Peter Bent Brigham Hospital.

Fig. 17. Robert Breck Brigham Hospital.

FIG. 18. ST. ELIZABETH'S HOSPITAL, BRIGHTON, MASS.

investigation in addition to those for the routine study of hospital patients.

The Massachusetts Homeopathic Hospital is a general hospital with Research, Maternity, Contagious and Out-Patient Departments. In addition, it maintains a small home, Sunnybank, for women convalescents, and assures the responsibility of supplying the Medical and Surgical staff for the Medical Mission Dispensary. It is the teaching hospital of Boston University School of Medicine. 530 beds, exclusive of those in its nurseries, are maintained. During 1927, 11,505 in-patients, of whom 1917 were maternity, were cared for and 57,980 visits were made to its Out-Patient Departments.

The New England Deaconess Hospital, (Fig. 14), of 181 beds is devoted equally to medicine and surgery. Adjacent to it and under similar management is the Palmer Memorial Hospital, (Fig. 15), of 75 beds for chronic disease especially cancer. During 1927 there were 4,937 patients admitted to the two hospitals. The laboratories are highly developed, and are closely coordinated with those of the Harvard Cancer Commission.

The Peter Bent Brigham Hospital, (Fig. 16), has 246 beds for general medical and surgical cases. It also maintains an Out-Door Department open all day long in which in 1927 there were 7699 new cases treated who made 60,671 visits. Besides laboratories for routine work there is extensive provision for medical investigation and laboratories in connection with hospital wards.

The Robert Breck Brigham Hospital, (Fig. 17), has 110 beds for the treatment of patients with chronic disease.

St. Elizabeth's Hospital, (Fig. 18), is a general hospital with 245 beds and a large Out-Patient Department.